

FEB 1 1923

VOLUME 3

NUMBER 2

ARCHIVES OF PATHOLOGY AND LABORATORY MEDICINE

EDITORIAL BOARD

LUDVIG H. EMMEN, Chicago

JAMES EWING, New York

WILLIAM THORNTON, Philadelphia

WILLIAM B. COOPER, Boston

J. A. MACCALLUM, Chicago

ALBERT J. COHEN, Philadelphia

FEBRUARY, 1923

OFFICIAL MONTHLY OF AMERICAN MEDICAL ASSOCIATION, 535 NORTH
DEARBORN STREET, CHICAGO, ILL. ANNUAL SUBSCRIPTION, \$5.00

Published by the American Medical Association, 535 North Dearborn Street, Chicago, Ill. Under the Act of Congress, October 3, 1917, Acceptance for mailing at special rate of postage provided for in the Act of October 3, 1917, authorized May 22, 1922.

NUMBER

1

and Technical Notes:

Native Descriptions of

Human Tissues. Also

W. H. and Arthur

Notes on the Tubercle

Charles White, M.D.,

the German Literature

Sections:

Society of Clinical Pathology

Society of Philadelphia

Pathological Society.

ARCHIVES OF PATHOLOGY

AND

LABORATORY MEDICINE

VOLUME 3

FEBRUARY, 1927

NUMBER 2

ANASTOMOSING BRONCHI IN THE HUMAN LUNG *

WITH FIVE PLATES

WILLIAM SNOW MILLER, M.D.

MADISON, WIS.

At the time I was studying pulmonary lymphoid tissue in old age¹ my colleague, Dr. C. H. Bunting, brought me a lung which he had removed from a woman 90 years and 7 months old. The following abstract is taken from the necropsy protocol.

The organs showed the atrophy and pigmentation of old age. The heart was the seat of mitral stenosis with some hypertrophy, and well marked dilatation of the right auricle and ventricle. There was marked coronary sclerosis, with calcification, and fibrous myocarditis. The aorta was dilated, tortuous, and showed extensive senile sclerosis. The lungs were emphysematous.

The woman was found dead in bed in the morning; and in the absence of any evidence of violence, acute inflammatory reaction, or any toxic activity, it was assumed that death was due to acute dilatation of the heart, either as the result of gastric distention, or of mental shock at the death of her son, which occurred in her presence the evening previous to her death.

Several series of sections were cut from different parts of the lung, but the presence of emphysema and a chronic bronchitis prevented the use of these sections in the study of lymphoid tissue.

In going over one of the series of sections, the peculiar appearance of certain of the bronchi attracted my attention and led to their being followed through the series, and eventually to their reconstruction.

It is unfortunate that the lung had been cut into before the blocks were cut out for embedding, for this prevented a further following of the bronchi; still, had the lung been intact, it is not improbable that blocks would have been cut from other portions of the lung and the peculiar arrangement of the bronchi have been missed.

* Aided by a grant from the National Tuberculosis Association.

* From the University of Wisconsin.

1. Miller, W. S.: The Pulmonary Lymphoid Tissue in Old Age, *Am. Rev. Tuberc.* 9:519, 1924.

The blocks were embedded in celloidin and cut serially, after the method of Obrega, and stained with haematoxylin and eosin. The series from which the reconstruction was made consisted of 300 sections fifty micra in thickness. The sections were drawn by means of an Edinger projection apparatus with an amplification of twenty-five diameters.

Briefly stated, the reconstruction showed two systems of branching and anastomosing bronchi which were at no point connected with each other. Each system had a peculiar bronchus which, as it was followed through the series of sections, bore a different relation to a branch of the pulmonary vein.

An extended search through the literature at my command failed to show any record of a similar modification of the bronchial tree. I am, therefore, compelled to confine myself to a detailed description of the bronchi as brought out in the reconstruction.

No attempt has been made to distinguish the various orders of the bronchi; throughout the following description they are designated as *B 1*, *B 2*, etc. Each figure will be described independently, and its position in the model can be found by reference to plates I and II.

In plate III, figure 1, the mucosa is thrown into regular folds. It is lined with a ciliated columnar epithelium which contains an unusual number of goblet cells whose mucous contents are being poured out in large quantities into the lumen of the bronchus. The bronchus is surrounded by well developed bands of smooth muscle. Outside of the muscle, in the connective tissue, there are numerous blood vessels packed full of blood, which apparently belong to the bronchial, rather than to the pulmonary, circulation. Near the center of the band of connective tissue extending between *B 1* and *B 2*, there is a small spicule of bone (*x*), and along its upper and lower border there are groups of mucous glands. The letter *B* which precedes all the figure numbers in the text is omitted in the illustrations. The narrow band of connective tissue which extends from the lower border of *B 1* is the continuation of the connective tissue about the pulmonary vein shown in text figure 1. Bronchus *B 2* possesses the same characteristics as *B 1*.

In figure 2, *B 1*, is no longer enclosed in a connective tissue sheath which is common to it and *B 2* but is still connected with the pulmonary vein by the band seen in text figure 1. Beyond this level *B 1* and *B 2* gradually pursue an independent course. The general structure of *B 1* is the same as in figure 1. The small spicule of bone seen in figure 1 has disappeared. At the extreme left, associated with the group of blood vessels, there is a small group of mucous glands, and just below the bronchus there is a small amount of lymphoid tissue. The blood vessels are numerous, and, like those in figure 1, probably belong to the bronchial circulation.

B 2 pursues a different course from that of *B 1*. It gives origin to a branch which first passes obliquely forward and then, turning at a sharp angle, it passes outward and backward eventually to form an anastomosis with *B 3*, which is a branch of the normal bronchial tree. The section of the bronchus, and its anastomosing branch *B 2a*, present a sinuous outline. It is lined throughout its course with ciliated columnar epithelium interspersed with many goblet cells which have emptied their secretion into the lumen of the bronchus. The musculature follows the sinuosities of the bronchial walls. The epithelium does not penetrate the musculature at any place. The connective tissue sheath which was primarily about *B 2* extends along the anastomosing

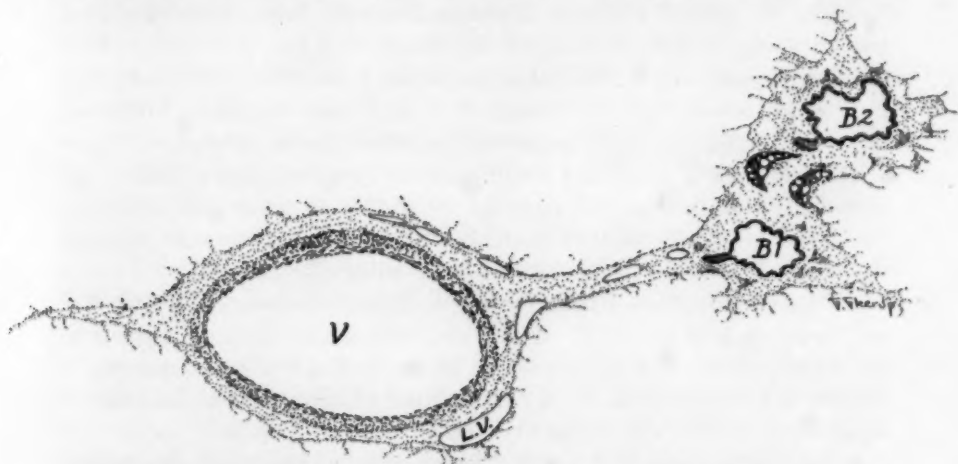


Fig. 1.—This figure shows the relation of *B 1* and *B 2* to the pulmonary vein and the band of connective tissue which extends between the vein (*V*) and the two bronchi. The clear openings in the connective tissue about the vein and in the band of connective tissue which extends between the vein and the two bronchi are lymph vessels (*L V*). Figure 1, plate III, shows the detail of the bronchi.

branch and joins that about *B 3*. There is the same arrangement of the blood vessels along the anastomosing branch as about *B 2*. A delicate strand of connective tissue extends obliquely from the lower portion of *B 2* and joins that which extends between *B 1* and the pulmonary vein.

B 3 is cut at the point where it is dividing; hence the irregular hour-glass outline of its section. On its inner side, situated in its connective tissue sheath, there is a well marked spicule of bone (x). This is the position in which a small rod of cartilage would be found in the normal lung of a younger person.

In figure 3, there is no noticeable change in the structure of *B 1*. The bronchus and pulmonary vein are gradually approaching each other, and, consequently, the band of connective tissue between the two

is shorter. Only a short length of the anastomosing branch, *B 2a*, remains connected with *B 2*. While the opening of *B 2a* into *B 3*, because of the arching of the bronchus, did not appear in figure 2, it is now seen in direct communication with that bronchus. The spicule of bone present in figure 2 extends into this section (*x*).

The epithelium presents an interesting study. In *B 2* and in *B 2a* it consists of columnar ciliated cells interspersed with numerous goblet cells. The same arrangement of epithelium is found in that portion of *B 3* into which *B 2a* opens; also directly opposite the entrance of *B 2a* into *B 3*; elsewhere in *B 3* the epithelium consists of ciliated cuboidal cells with few goblet cells. Tall columnar ciliated epithelium, containing a large number of goblet cells, is characteristic of these branching and anastomosing bronchi throughout the series.

The section in figure 4 is taken below the point where the anastomosing branch which extends from *B 2* to *B 3* joins the latter bronchus. All the bronchi appear in transverse section. In the connective tissue at the left of *B 2* there is a small mass of lymphoid tissue, and a still larger mass is seen at the right of *B 3*. These masses of lymphoid tissue are not connected with each other; they are, like normal lymphoid tissue, situated in the angle formed by dividing bronchi.

A narrow band of connective tissue extends between *B 1* and *B 2* and between *B 2* and *B 3*. The main vein, which does not appear in the figure, gives off a branch which arches to the left and comes to lie a short distance below *B 2*. A narrow band of connective tissue extends between *B 2* and the connective tissue about this vein.

The epithelium in *B 1* and *B 2* is the characteristic ciliated columnar epithelium with a large number of goblet cells, while that in *B 3* is ciliated cuboidal epithelium with but few goblet cells.

In figure 5, as *B 3* has no further connection with *B 2*, it is omitted from the remaining illustrations; it can, however, be followed out in the reconstruction, plates I and II.

In this figure the plane of section passes through the point where the anastomosing branch *B 1a* leaves *B 1*. The anterior extension of *B 1* is the beginning of the anastomosing branch, and, as in normal bronchi, there is a small amount of lymphoid tissue in front of and behind the place where the anastomosing branch leaves *B 1*. There is a small group of mucous glands in the connective tissue at the left of the bronchus. The epithelium has the same characteristics as in the preceding sections. *B 2* presents an elongated, flattened outline; otherwise it has the same structure as in the preceding sections.

The vein which was mentioned in connection with figure 4 gives off a branch which occupies a position between *B 2* and *B 3* in this section. Beyond this point no branch of either the pulmonary vein or pulmonary artery is found near *B 2*.

The section in figure 6 cuts through *B 1* below the origin of the anastomosing bronchus *B 1a*. The bronchus has a circular outline with two, rather deep, outfoldings in its mucosa. A narrow band of connective tissue extends between *B 1* and *B 2*.

The outline of the section of *B 2* has widened out from that of figure 5. These variations in outline are a feature of the anomalous bronchi, and they give rise to the irregularities seen along their reconstruction, plates I and II. Around the outfolding of the mucosa, seen on the upper left portion of the bronchus, there is a small mass of lymphoid tissue. The blood vessels are more prominent than in some of the preceding sections.

The anastomosing branch *B 1a* which connects *B 1* and *B 4* has an oblique direction. As it leaves *B 1* it is smaller than that bronchus, and has for a short distance a tubular form which soon assumes a compressed fusiform outline that is maintained until it joins *B 4*. It is lined throughout with ciliated columnar epithelium interspersed with goblet cells which are less numerous than in *B 1*. This anastomosing bronchus, like that extending between *B 2* and *B 3*, is surrounded throughout its entire course by bands of smooth muscle. There is a narrow band of connective tissue extending between *B 1a* and *B 4*. Histologically, *B 4* does not differ in any respect from a normal bronchus.

In plate IV, figure 7, the only noticeable change from figure 6 in *B 1* or *B 2* is the presence of a small spicule of bone (*x*) in the connective tissue about *B 1*. This extends as far back through the intervening sections as the angle formed by the giving off of *B 1a* from *B 1*, and corresponds to the position a cartilagenous plate, or rod, would occupy in a normal lung.

The plane of this section cuts through the small, downward, projection in *B 1a* and through the junction of *B 1a* with *B 4*. The ciliated columnar epithelium lining *B 1a* contains fewer goblet cells than *B 1*, and they are practically absent from the epithelium lining *B 4*. In *B 1* and *B 2* the goblet cells are as numerous as in the first section of the series.

If the section in figure 8, had been the only one studied, it would not have been difficult to distinguish the two abnormal bronchi from the normal bronchus. The close relationship of *B 1* to the pulmonary vein and the unusual position of *B 2* unaccompanied by a branch of the pulmonary artery would attract attention. The presence of an unusual number of goblet cells would also distinguish *B 1* and *B 2* from *B 4*, which belongs to the normal bronchial tree. The character and size of the pulmonary alveoli present nothing noticeable.

Neither *B 1* nor *B 2* appear in any of the illustrations beyond this point. The flattened outline of *B 2* persists for some distance beyond

this section; it then gradually changes to the outline seen in text figure 2. Throughout its entire extent it is neither directly nor indirectly connected with any alveoli. *B 1* gradually changes its position to one directly in front of the pulmonary vein; then to one at its right, and finally it divides into the two branches shown in plate II.

A new bronchus enters into figure 9: namely, *B 6*. There can also be seen a small portion of still another bronchus, *B 4a*, above and to the left of *B 4*. Both *B 4* and *B 6* belong to the normal bronchial tree; but *B 4a* is an anastomosing bronchus which extends between *B 4* and *B 5*, and *B 6* is a subdivision of *B 5* (plate II).

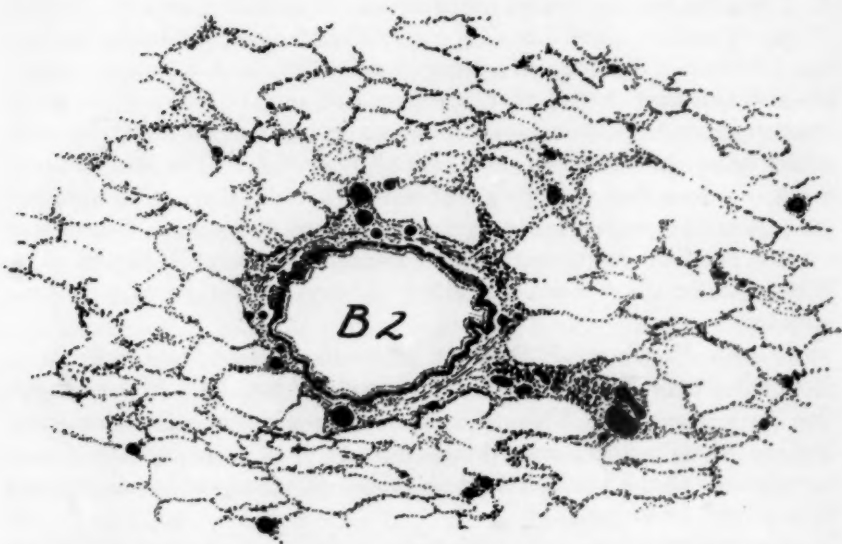


Fig. 2.—This figure shows the relations of *B 2* in the last section of the series. Such blood vessels as are present probably belong to the bronchial circulation.

There is a difference in the type of epithelium lining *B 4* and *B 6*. In *B 4* the epithelium is a ciliated columnar epithelium with but few goblet cells, while in *B 6* it is a ciliated cuboidal epithelium in which no goblet cells are present. This shows that they belong to different orders of bronchi.

The only difference between figure 10 and figure 9 is that the plane of section cuts through the opening of *B 4a* into *B 4*. There is no sharp differentiation between the epithelium in *B 4* and that in *B 4a*. In each bronchus the epithelium is ciliated and contains but a few goblet cells. There is no change in the character of the epithelium in *B 6* from that in figure 9.

In figure 11, the plane of section passes through *B 4a* after it has lost its connection with *B 4* and at the point at which *B 6* and *B 7* are given off from *B 5*. The plane of the section in figure 12 lies through *B 4*, *B 4a*, *B 5* and *B 7*. Both *B 4* and *B 5* are lined with ciliated columnar epithelium, the individual cells being of the tall columnar type. On the other hand in *B 4a* and *B 7* the epithelium is of the cuboidal type.

Included in the section in figure 13, plate 5, are *B 4*, *B 4a* at its junction with *B 5*, and *B 7*; the latter bronchus is dividing into two bronchioli respiratorii. The epithelium lining *B 7* is still ciliated cuboidal epithelium, but becomes a simple nonciliated cuboidal epithelium and, finally, a much flattened squamous epithelium at the beginning of the bronchioli respiratorii. The epithelium lining the other bronchi remains the same as in the preceding figure. The branch of the pulmonary artery which accompanies *B 7* and the subdivisions of the bronchioli respiratorii appear in this section.

The continuation of *B 4* with its accompanying artery, and of *B 5* appear on the right of the section in figure 14. The bronchus, *B 7*, is the most interesting feature in the section, because all of the ultimate subdivisions of the bronchial tree can be recognized in one of its branches. In that branch of *B 7* which passes obliquely upward and to the left, a short portion of a bronchiolus respiratorius (*b. r.*) can be identified; this divides into two ductuli alveolares (*d. al.*). The uppermost of these two is cut lengthwise, and an atrium (*a.*) with a single sacculus alveolaris (*s. al.*) appears as a direct continuation of the ductulus. Sections of the branch of the pulmonary artery which accompanies the ductulus can be seen along its left side. The distal wall of the sacculus alveolaris lies in close contact with a branch of the pulmonary vein (*v.*), showing that this is the boundary of a primary lobule.

In the bronchiolus respiratorius the epithelium is a simple cuboidal epithelium where it leaves *B 7*; it then flattens out, and in the remaining portion of the bronchiolus respiratorius, the ductuli alveolares, the atria and the sacculi alveolares, it is a simple squamous epithelium (respiratory epithelium).

In the section in figure 15 *B 5* is somewhat flattened, and is cut a short distance above its origin from the bronchus indicated by an asterisk in plate II. This bronchus, because of its situation at the extreme edge of the sections, could not be followed for any distance.

The bronchus *B 4* is cut where it gives origin to two smaller bronchi which are situated nearly opposite to each other, and to a third branch, *B 10*, figure 16, which does not appear in this section. There is a pronounced expansion of *B 4* at the place where these bronchi are given off. A portion of this expansion is seen in figure 15 and in plate II.

Both of the bronchi which arise from *B 4* are lined with ciliated cuboidal epithelium; this becomes a nonciliated cuboidal epithelium as

the end of the longer branch (left in plate II, lower in fig. 15) is approached. The two expansions, one on either side of this bronchus, indicate the points at which the bronchioli respiratorii arise. The distal end of this branch also ends in a bronchiolus respiratorius.

The bronchus *B 8* appears for the first time in this section. Sections of its accompanying artery are seen below, and at its right. This bronchus will be discussed in detail in connection with figures 16 and 17.

Two new bronchi are present in the section in figure 16, *B 10* and *B 9*; the latter of these is a short bronchus that extends between *B 10* and *B 8*. It is questionable whether, as stated under figure 15, *B 10* represents a branch of *B 4* or a direct continuation of that bronchus. On the one hand it is lined with ciliated cuboidal epithelium, just as are the two branches which appear in figure 15; on the other hand, it is a much larger bronchus than either of the two branches described, and itself gives rise to a branch, *B 9*. Taking all the factors into consideration, *B 10* probably represents a direct continuation of *B 4*, although the series does not extend far enough to enable one to make a positive statement.

The artery which gives origin to the branches that accompany *B 8* in figure 15 is situated above and to the right of *B 8*, while the artery accompanying *B 10* is situated on its left side. Neither of these arteries is included in figure 16.

In the section in figure 17, *B 10* is cut below the level at which *B 9* is given off; but a small portion of the latter bronchus is included in the section of *B 8*.

It is interesting to note that *B 9*, in its relation to *B 8*, is comparable to *B 7* in figure 14, where, at the level that bronchioli respiratorii are given off from *B 7* a wide dilatation is seen. The same condition, only on a larger scale, is seen in *B 8*, figure 17.

The type of epithelium differs in that portion of the section which belongs to *B 9* from that portion belonging to *B 8*. In *B 9* it is a ciliated cuboidal epithelium, while in *B 8* it is a nonciliated cuboidal epithelium. Two bronchioli respiratorii arise from *B 8*; one of them can be followed to its termination in a ductulus alveolaris.

On the right side of *B 8* the accompanying pulmonary artery is cut obliquely. Two branches of this artery appear in figure 15 in close proximity to *B 8*. A small branch of this artery that accompanies the ductulus alveolaris in figure 17 is seen on the left of the ductulus.

COMMENT

Two theories may be advanced to explain these anastomosing bronchi, namely: (1) they are bronchiectases; (2) they are a part of a fetal anomaly which has persisted to extreme old age.

Two types of bronchiectases can, in general, be recognized—a cylindric and a saccular. In the cylindric type, abnormally wide channels are formed in the lung by the dilatation of normal bronchi. These channels may be occasioned by an incomplete obstruction of a bronchus, that leads to the dilatation of its more distal branches, or it may be due to an atelectasis. In the later case, the lung probably became compressed early in life.

In the sacculated type the dilatations are sometimes of great size, and usually communicate with one side of a bronchus, the opening which leads into the dilatation being situated between the bands of smooth muscle which belong to the bronchus. In sections which are cut through the center of one of the openings, the thickened muscle can be seen on either side of the opening. Sometimes there are a number of these sacculated dilatations along a bronchus, giving to it a beaded appearance.

Neither *B 1* nor *B 2* possess any of the characteristics of a bronchiectasis. There is only one place in the reconstruction of the bronchi where there is anything that suggests a bronchiectasis, and that is the somewhat flattened fusiform dilatation (*B 1a*) which extends between *B 1* and *B 4*. This dilatation, however, has its own musculature and is lined throughout with ciliated columnar epithelium, interspersed with goblet cells; moreover, this fusiform dilatation is, in reality, an anastomosing bronchus which extends between an abnormal bronchus and a normal bronchus and partakes of the character of the former, rather than of the latter, bronchus. The dilated bronchioli and bronchioli respiratorii are not to be considered as bronchiectases, but as part of the emphysema present throughout the lung. They are usually involved in the emphysema of old age. The theory that these structures represent bronchiectasiae appears untenable.

It is unfortunate, as has been stated, that the lung had been cut into before it came into my possession, and that a larger block had not been removed for sectioning. No one, however, could have foreseen in the gross specimen the condition revealed by the serial sections, for it presented no indication of the condition either to sight or to touch.

As soon as the peculiar bronchi were recognized a careful, but unsuccessful, search was made for any remaining portions of *B 1* and *B 2* in the gross specimen. Numerous series were cut and in one of them what might have been a possible continuance was found; but the interval between the two series was so great that only by a vivid imagination could the two be connected. It is possible that in leveling off the top of the block for sectioning the series sufficient material was removed to change the character of the sections.

That these bronchi represent bronchiectases has been shown to be untenable. The other theory remains: namely, that the bronchiectases represent the remains of a fetal anomaly.

In text figure 1, the general relation of the two bronchi *B 1* and *B 2* as found in the first section of the series is shown. In the normal lung the various divisions of the bronchial tree are closely associated with corresponding subdivisions of the pulmonary artery, and they exceed in diameter the associated artery, except near the hilum of the lung, where they are often of equal size. In the present instance the bronchi are associated with a branch of the pulmonary vein rather than with a branch of the pulmonary artery, and the vein has a far greater diameter than either of the two bronchi.

The bronchus designated as *B 1* in text figure 1 and the pulmonary vein gradually approach each other; and in the last section of the series the vein, reduced in diameter, occupies a position between the two branches into which *B 1* has divided. On the other hand, the bronchus designated as *B 2* does not divide, but becomes further removed from the vein; accompanied by its own sheath of connective tissue in the last section of the series (text fig. 2), unaccompanied by either pulmonary artery or vein, it is surrounded by pulmonary alveoli with which it has no connection at any point along its course.

From the foregoing analysis of the reconstruction it appears that the second theory, that these branching and anastomosing bronchi represent a fetal anomaly, gives the most satisfactory explanation.

PLATE I

Fig.
1

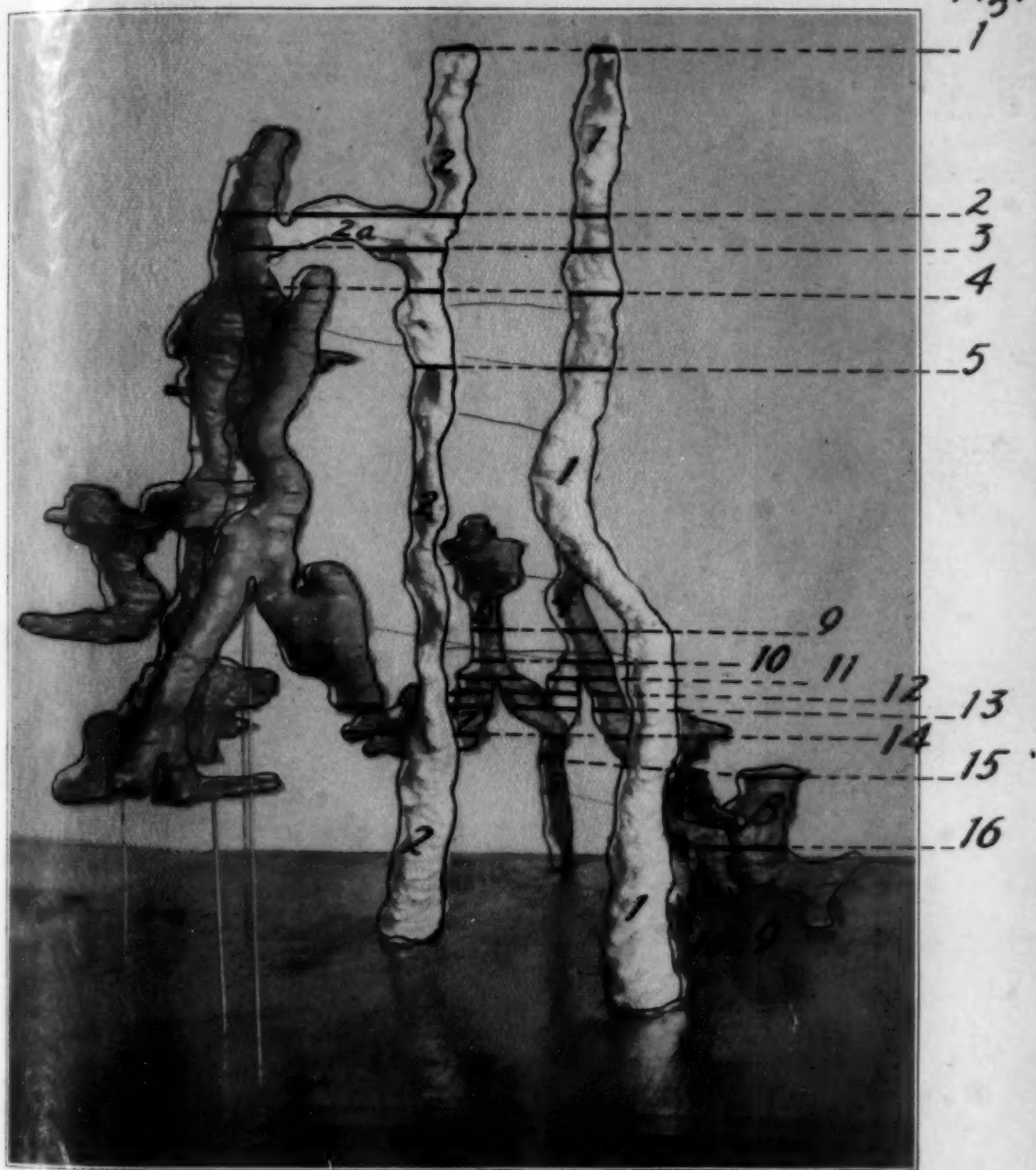


Plate I.—Posterior view of the reconstruction. The normal bronchi, and their extensions, are colored yellow, the abnormal, white. In plates I and II, the plane of the section is indicated by the solid line; the leaders, by broken lines.

Fig. 1
 In text figure 1, the general relation of the two bronchi *B 1* and *B 2* as found in the first section of the series is shown. In the normal lung the various divisions of the bronchial tree are closely associated with corresponding subdivisions of the pulmonary artery, and they exceed in diameter the associated artery, except near the hilum of the lung, where they are often of equal size. In the present instance the bronchi are associated with a branch of the pulmonary vein rather than with a branch of the pulmonary artery, and the vein has a far greater diameter than either of the two bronchi.

5
2
4
2
 The bronchus designated as *B 1* in text figure 1 and the pulmonary vein gradually approach each other, and in the last section of the series the vein, reduced in diameter, occupies a position between the two branches into which *B 1* has divided. On the other hand, the bronchus designated as *B 2* does not divide, but becomes further removed from the vein; accompanied by its own sheath of connective tissue in the last section of the series (text fig. 2), unaccompanied by either pulmonary artery or vein, it is surrounded by pulmonary alveoli with which it has no connection at any point along its course.

From the foregoing analysis of the reconstruction it appears that the second theory, that these branching and anastomosing bronchi represent a fetal anomaly, gives the most satisfactory explanation.

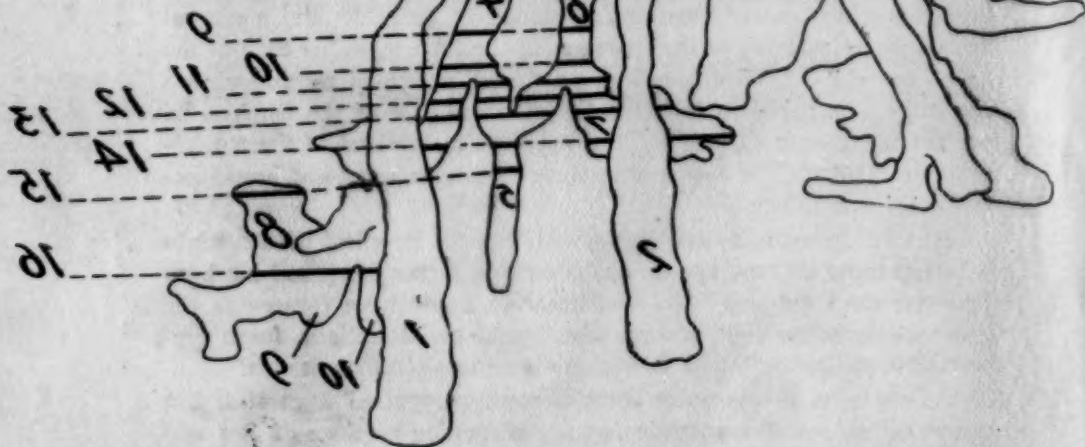


PLATE I

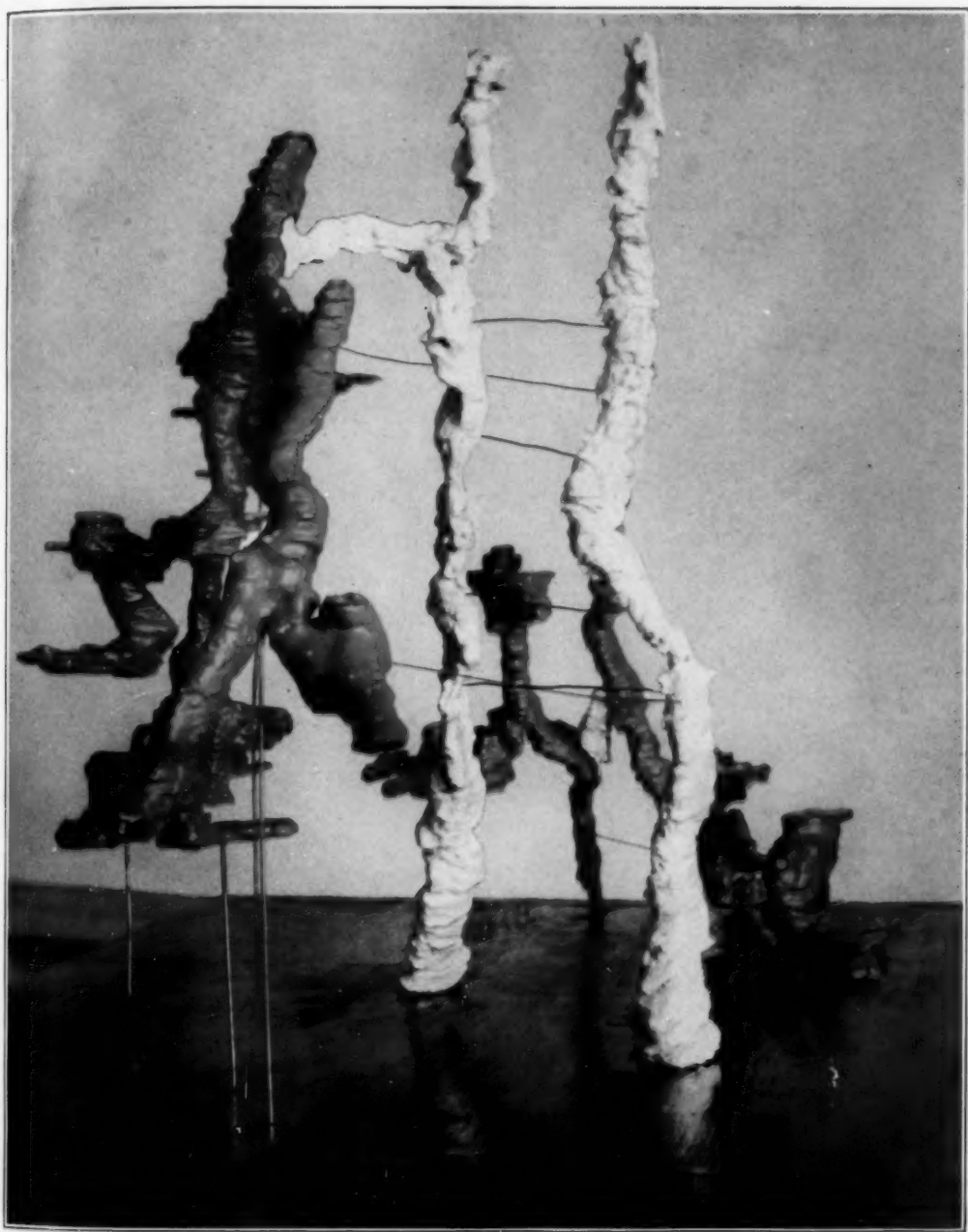


Plate I.—Posterior view of the reconstruction. The normal bronchi, and their extensions, are colored yellow, the abnormal, white. In plates I and II, the plane of the section is indicated by the solid line; the leaders, by broken lines.



PLATE II

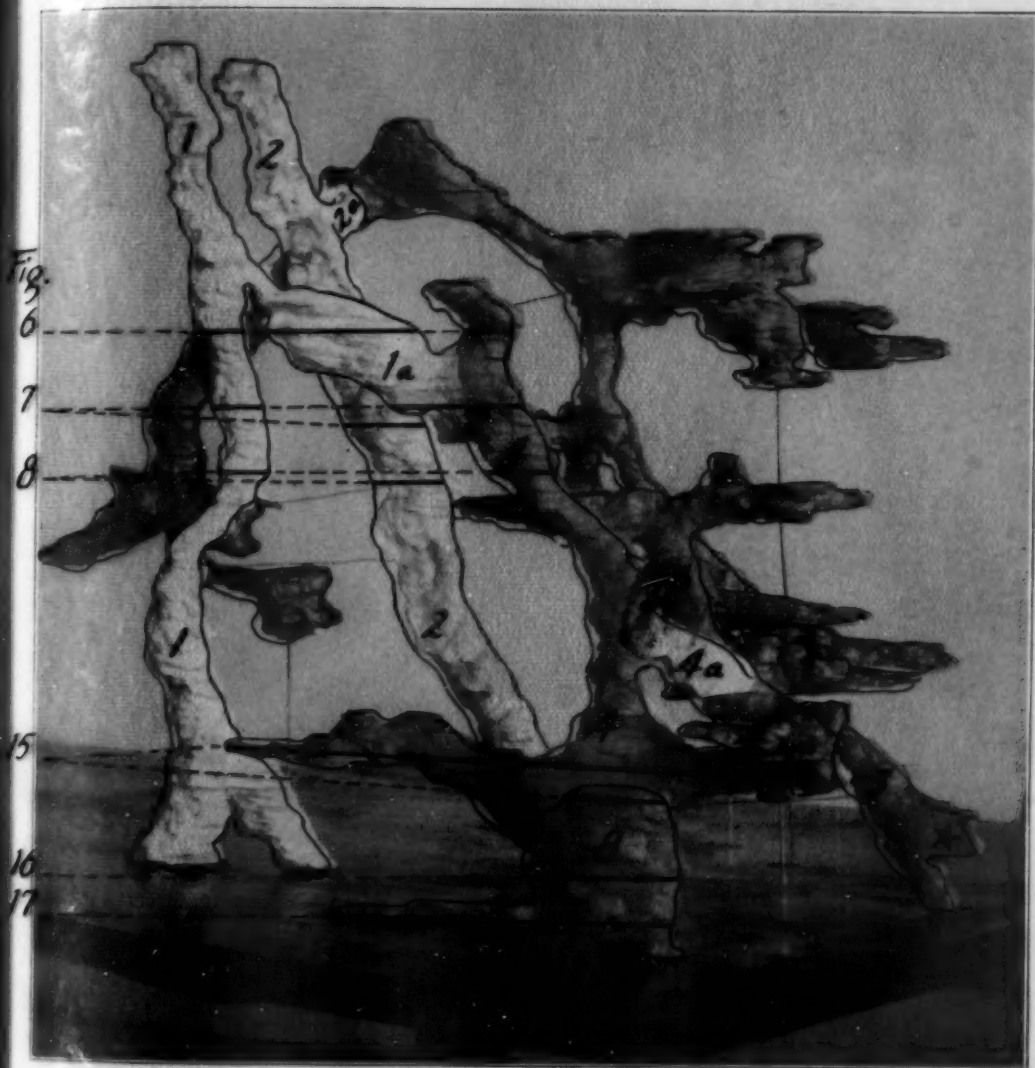


Plate II.—Lateral view of the reconstruction. Colors as in plate I.

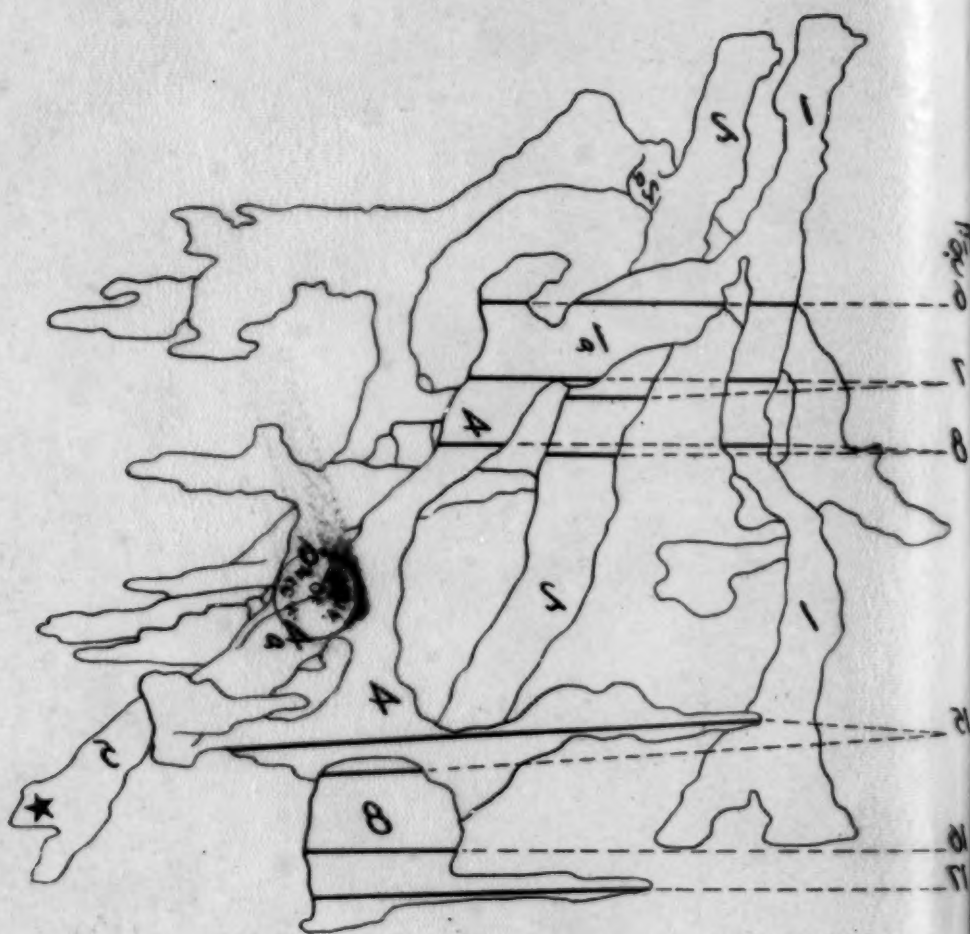


PLATE II

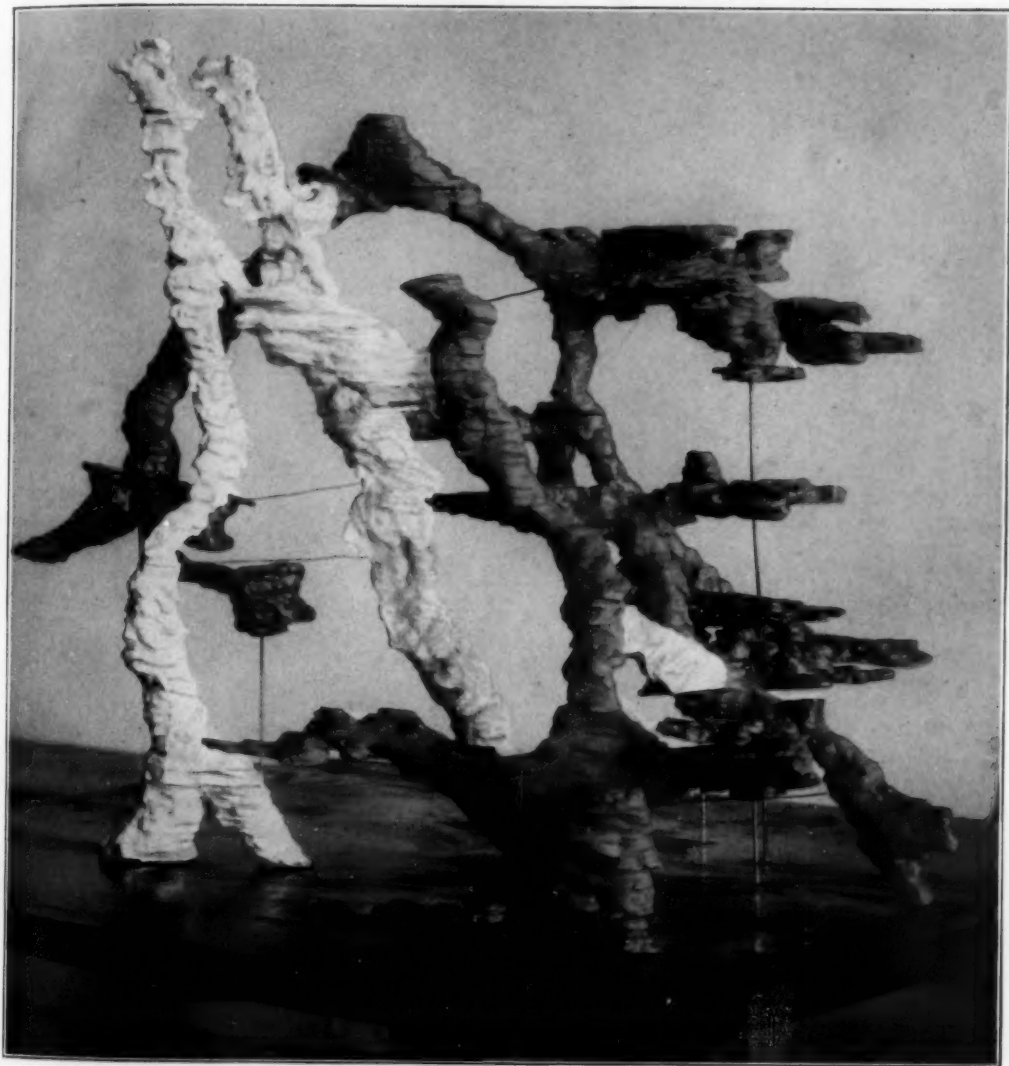


Plate II.—Lateral view of the reconstruction. Colors as in plate I.



PLATE III

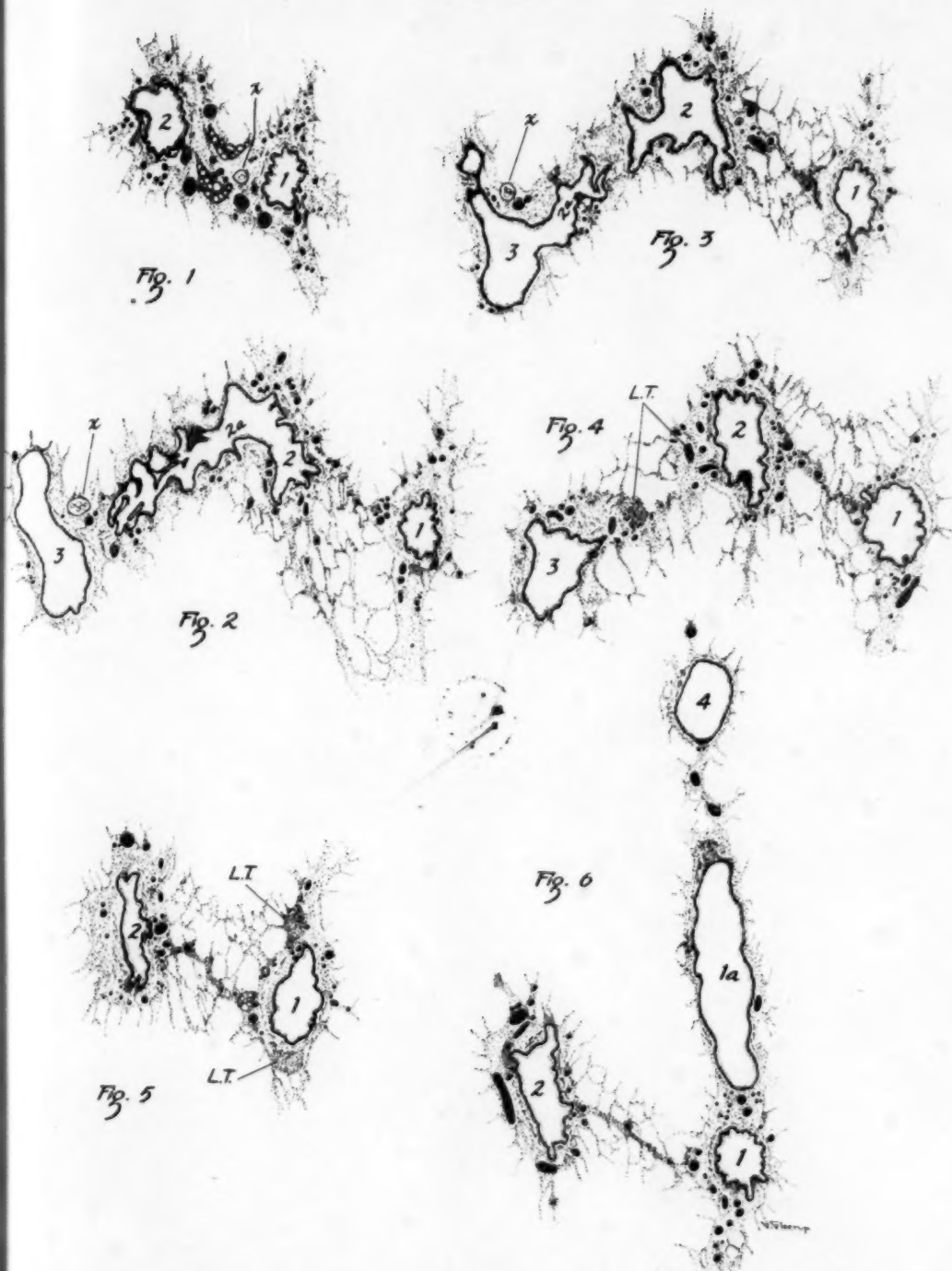


Plate III.—In this plate and in plates IV and V, the figures are numbered consecutively. The bronchial blood vessels, and pulmonary veins, are in solid black; the pulmonary artery is in outline. Full description of each figure is given in the text. Figure 1 is the first section of the series; figure 2, taken 2.8 millimeters below figure 1; figure 3, taken 150 microns below figure 2; figure 4, taken 200 microns below figure 3; figure 5, taken 650 microns below figure 4; figure 6, taken 800 microns below figure 5.

PLATE IV



Plate IV.—Figure 7, taken 650 microns below figure 6; figure 8, taken 700 microns below figure 7; figure 9, taken 3.15 mm. below figure 8; figure 10, taken 200 microns below figure 9; figure 11, taken 250 microns below figure 10; figure 12, taken 500 microns below figure 11.

PLATE V

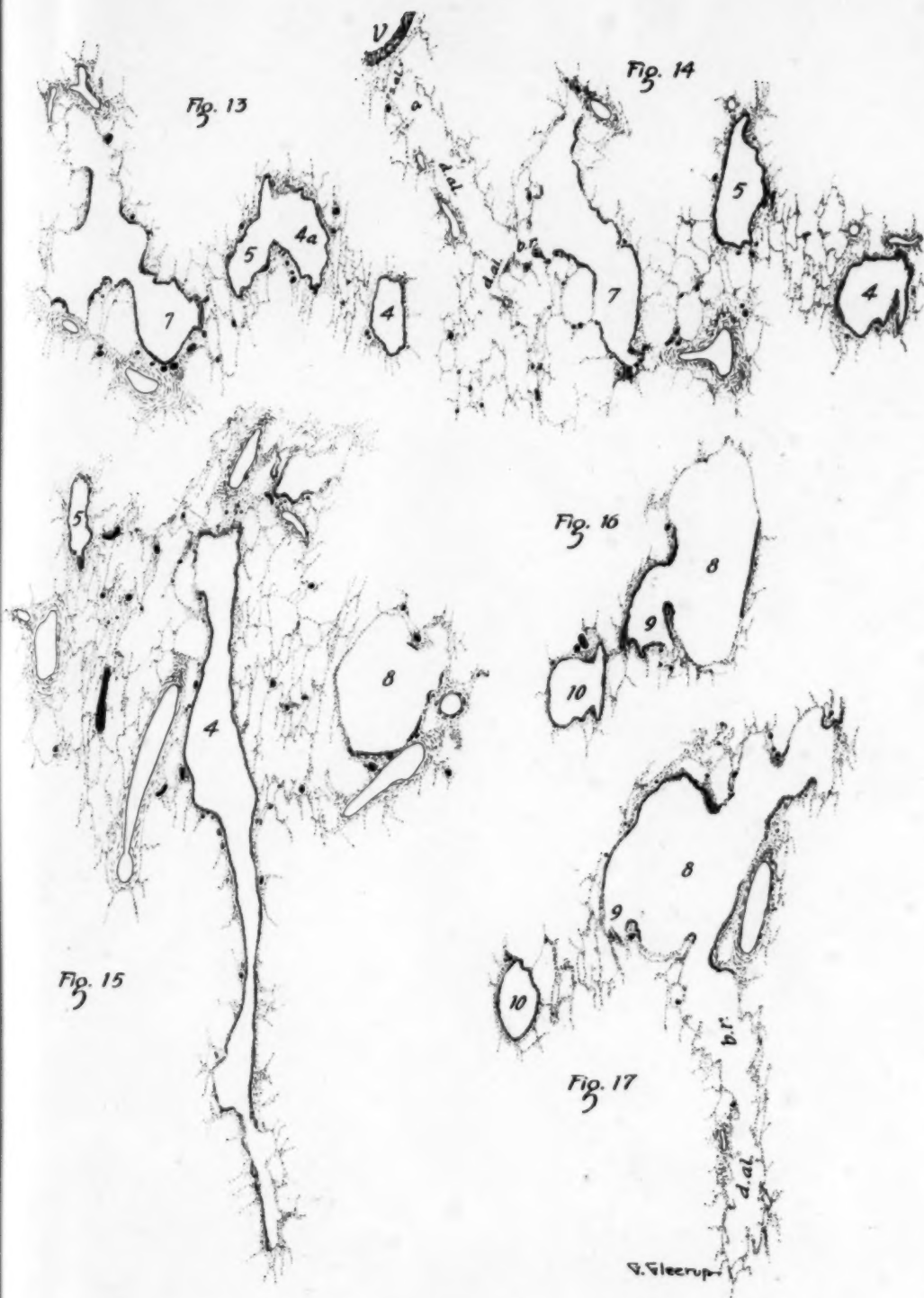


Plate V.—Figure 13, taken 200 microns below figure 12; figure 14, taken 500 microns below figure 13; figure 15, taken 1 mm. below figure 14; figure 16, taken 1.2 mm. below figure 15; figure 17, taken 800 microns below figure 16.



PYGOPAGUS TWINS

THE HISTORY AND NECROPSY REPORT OF THE BOHEMIAN
TWINS, ROSA-JOSEPHA BLAZEK *

M. A. PERLSTEIN, M.D.

AND

E. R. LECOUNT, M.D.

CHICAGO

Pygopus twins have been rare. Adolph,¹ in 1894, found records of twelve cases; Jacobi,² one year later recorded fourteen, and Hübner,³ in 1911, recorded twenty. In 1924, Géniaux⁴ reported another set of such twins. In these four articles there are mentioned altogether twenty-three such twins, the authenticity of three being doubtful. The following list is arranged chronologically.

1. The Biddenden Maids, born 1100, died 1134. It is doubtful whether these were pygopagi, although Ballantyne⁵ thinks that they were.

2. Female pygopagi reported by Ambroise Paré;⁶ born in 1475, "lived for quite a while."

3. Male pygopagi reported by Paré⁶ and Licetus;⁷ born in 1486. We have not been able to find out how long these twins lived.

4. Female pygopagi reported by Treyling;⁸ born in 1700, died four months later, following their surgical severance.

5. Helena-Judith, the Hungarian sisters, reported by Torkos⁹ and by Werther;¹⁰ born in 1701, died in 1723.

* From the Pathological Laboratories of the Rush Medical College of the University of Chicago.

1. Adolph, F.: *Ein menschlicher Pygopus*, Inaugural Dissertation, Marburg, Pathologic Institute, 1894.

2. Jacobi, A.: Dr. S. Tynberg's Pygopus, *Arch. Pediat.* **12**:721-729, 1895; A Correction, *ibid.* **13**:20, 1896.

3. Hübner, Hans: *Die Doppelbildungen des Menschen und der Tiere*, *Ergebn. d. allg. Pathol. u. path. Anat.* **15**:1-348, pt. 2, 1911.

4. Géniaux, H.: Un pygopage masculin, observé à Camp Boulhaut (Maroc occidental) en Janvier, 1914, *Monde méd.* **34**:595-599, 1924.

5. Ballantyne, J. W.: The Biddenden Maids; the Mediaeval Pygopus (?) Twins, *Teratologia* **2**:268-274, 1895.

6. Paré, Ambroise: *Opera*, Paris, J. Dupuys, 1582, p. 734, cited by Jacobi (footnote 2).

7. Licetus, F.: *De monstribus*, Amsterdam, sumpt. A. Frisii, 1665, p. 80, cited by Hübner (footnote 3).

8. Treyling, J. J.: *Gemellae mediantibus ossibus coccygis sibi invicem connatae*, *Acta Physico-Medica Acad. Caesareae Leopoldino-Carolinae, Nat. Curios. Exhibentia* 1740, *Ephemerides* **5**:445, cited by Hübner (footnote 3).

9. Torkos, J. J.: *Observationes anatomico-medicae de monstro bicorporeo virgineo*, *Phil. Tr.*, London **50**:311-322, pt. 1, 1758-1759.

10. Werther, G. C.: *Disputatio medica de monstro Hungarico*, Lipsiae, 1707, cited by Hübner (footnote 3).

6. Pygopagus twins reported by Wolff;¹¹ sex not mentioned, born 1778, lived two months.

7. Male pygopagi reported by Normand;¹² born 1818, lived nine days.

8. Female pygopagi reported by Molitor;¹³ born 1826, lived twenty-five days.

9. Female pygopagi reported by Barkow¹⁴ and Taruffi;¹⁵ born dead in 1828.

10. Chrissie-Millie, the African twins, reported by Ramsbotham,¹⁶ Virchow,¹⁷ and Rodriguez;¹⁸ female pygopagi; born 1850, died 1889.

11. Female pygopagi reported by Joly and Peyrat;¹⁹ born 1869, lived for a short (unspecified) time.

12. Rosa-Josepha Blazek, with whom this paper is chiefly concerned, born 1878.

13. Pilat²⁰ reported the birth of a child (sex not mentioned) with a mass which had undergone fatty degeneration attached to its sacral region. He believes that this mass represented the remains of a dead pygopagus twin. Nevertheless, this case must be considered as doubtful.

14. Male pygopagi, reported by Grosse;²¹ delivered by embryotomy in the eighth month of pregnancy, in 1885.

15. Male pygopagus reported by Bellert;²² born 1891, lived two months. This was a parasitic pygopagus, and therefore must be classed with the doubtful cases.

11. Wolff, C. F.: *Acta Acad. Scientiarum Petropol.* 1:41, 1778, cited by Jacobi (footnote 2).

12. Normand: *Observation sur deux jumeaux accolés dos à dos*, *Bull. de la Faculté de méd. de Paris*, 1818, no. 1, cited by Jacobi (footnote 2).

13. Molitor: *Beob. u. Abh. aus d. Gebiete d. ges. prakt. Heilk. v. oesterreich. ärzten*, Vienna, 1826, vol. 5, cited by Jacobi (footnote 2).

14. Barkow, J. C. L.: *Monstra animalium duplicia per anatomem indigata*, Lipsiae, 1828-1836. The description of their union is reprinted in Ernest Schwalbe's: *Die Morphologie der Missbildungen des Menschen und der Tiere*, Jena, Gustav Fischer, 1907, pt. 2, p. 249.

15. Taruffi, C.: *Storia della teratologie*, Bologna, reg. tip., 1882, vol 2, p. 398. This is an abstract of the report of Barkow.

16. Ramsbotham, F. H.: *A Description of the United African Twins*, *Chrissie-Millie*, *M. Times & Gaz.* 11:313, 1885.

17. Virchow, R.: *Ueber die sogenannte "zweiköpfige Nachtigall"*, *Berl. klin. Wchnschr.* 10:97-100, 1873.

18. Rodriguez, J. M.: *Noticias relativas á Millie-Chrissie*, etc., *Gac. méd. de México* 31:295-307, 1894.

19. Joly, N., and Peyrat, A.: *Études sur un monstre humain bifemelle du genre pygopage*, *Bull. Acad. de méd., Paris* 3:51-56, 1874.

20. Pilat: *Hydrops des Amnion, Zwillingschwangerschaft. Pygopagus. Tod des einen Foetus mit fettiger Degeneration desselben.*, *Ann. de gynec. et d'obst.*, August, 1879; *abstr.*, *Zentralbl. f. Gynäk.* 3:583, 1879.

21. Grosse: *Geburt eines zusammengewachsenen Zwillings*, *St. Petersburg. med. Ztschr.*, 1885, no. 10; *abstr.*, *Zentralbl. f. Gynäk.* 9:752, 1885.

22. Bellert: *Report of a Monstrous Child*, *Med. Obozr.* 35:830 and 36:285, 1891.

16. Female pygopagi reported by Marchand²³ and by Adolph;¹ born dead in 1894.
17. Lassen-Elaoussin, male pygopagi seen by Géniaux⁴ in 1914. At that time they were about 20 years old.
18. Tynberg's pygopagus, reported by Jacobi² and by Tynberg;²⁴ females born 1895, lived five months.
19. Strassmann's²⁵ case; pygopagi born dead in 1905.
20. Female pygopagi reported by Carmichael;²⁶ born 1906, died after an unspecified time.
21. Samar twins, reported by Rigall,²⁷ Plaggemeyer²⁸ and Van Denburg;²⁹ males, born 1908, still living in 1920.
22. Hilton twins, reported by Rooth³⁰ and Bockenheimer;³¹ female twins, born in 1908, and still living.
23. Female pygopagi reported by Achren;³² born in 1909, and 6 months old at the time reported.

In pygopagus twins, so far as we have been able to ascertain, the sex is always identical, a condition which has been attributed to their unioval embryogenesis. Of these twenty-three pairs of twins, fourteen were female and six male, and in three cases, those reported by Wolff,¹¹ Pilat²⁰ and Strassmann,²⁵ the sex was not stated. For this predominance of females, we have been unable to find an explanation. Pygopagus twins, as a rule, are more viable than other types of united twins, such as the craniopagus, thoracopagus or ischiopagus. Perhaps this is because the union in pygopagi involves no vital organs and, moreover, allows a carriage nearer the normal. Only four of these twenty-three pairs of twins were dead at birth. Of the remaining nineteen, five lived for short, unspecified periods, one lived for nine days, another for twenty-five days, two for two months, one for four months, one for five months and one for at least six months; the Samar twins were 12 years old in 1920, the

23. Marchand, F.: Ein menschlicher Pygopagus, Beitr. z. path. Anat. u. z. allg. Pathol. **17**:137, 1895.

24. Tynberg, S.: A Case of Pygopagus, Am. J. Obst. **32**:426-429, 1895.

25. We have been unable to confirm this reference cited by Hübner (footnote 3).

26. Carmichael, D. G.: United Female Twins, Brit. M. J. **1**:1352, 1910.

27. Rigall, R. M.: Samar Twins, Brit. M. J. **1**:1050, 1910.

28. Plaggemeyer, H. W.: A Urologic and Radiographic Study of the Samar Twins, Surg. Gynec. Obst. **30**:269-272, 1920.

29. Van Denburg: Godino Twins, California & West. Med. **22**:514, 1924.

30. Rooth, J.: A Case of United Twins, Proc. Roy. Soc. Med., Section on Diseases of Children **2**:242-246, 1908-1909; The Brighton United Twins, Brit. M. J. **2**:653-654, 1911.

31. Bockenheimer, P.: Vorstellung der zusammengewachsenen Kinder, Daisy und Violet Hilton, München. med. Wchnschr. **58**:2417-2418, 1911.

32. Achren, A.: Ein zusammengewachsenes Zwillingpaar (Schwedisch), Finska läk.-sällsk. handl., December, 1919; abstr., Gynäk. Rundschau **4**:540-541, 1910.

Hilton twins are 18 at present, the twins reported by Géniaux were about 20 in 1914, Helena-Judith died at the age of 22, the Biddenden Maids died at 34, Chrissie-Millie died at 38, and the Blazek twins died at the age of 43. Necropsies were performed in only five of these cases, and have been recorded by Treyling,⁸ Torkos,⁹ Barkow,¹⁴ Marchand²³ and Jacobi.² In the following account, the details of the necropsy of the Blazek twins are given. We have included, also, a review of the other articles which we were able to find regarding them, and believe that this paper may be among the last to be written concerning them.

ROSA-JOSEPHA BLAZEK

History.—Rosa and Josepha Blazek were born in Skreychov, Bohemia, on Jan. 20, 1878. The labor took place without any difficulty, and the mother was attended by a midwife. The mechanism of the labor was such that Rosa's head and shoulders were born first, followed by Rosa's trunk and Josepha's legs, and then by Rosa's legs and Josepha's trunk, and finally by Josepha's head. The occurrence of a similar mechanism in the delivery of five other pygopagi has been noted in three instances by Playfair,³³ in one by Rooth³⁶ and Bockhenheimer³⁵ and in one by Achren.³⁴ This mechanism occurs also in about 21 per cent of normal nonunited twins (Leonhardt³⁴). According to the father, there were two placentas and two cords, a condition also reported by Joly and Peyrat¹⁹ in two other sets of pygopagus twins. It follows that if "monstra duplicia come from one ovum,"³⁵ the prevalent belief that "the placenta in unio twins is always single"³⁶ is not borne out.

The Blazek twins were the second of four pregnancies. A sister one year their elder, in 1903 was living and well and the mother of four normal children, no twins. A brother, ten years their junior, was also living and well in 1922. A sister, the youngest in the family, succumbed to diphtheria in childhood. When the twins were born, the mother was 22 years old, the father 38. They and their families had lived in Bohemia as long as they could remember,³⁷ and there was no history of the birth of twins in either of their families.

The parents were apparently well at the time of the birth of the twins. Twenty-five years later, however, the mother had an apoplectic attack and a painless, crescentic ulcer of the leg which disappeared following the administration of potassium iodide. At that time, the father admitted a previous syphilitic infection. Whether or not this infection existed before the birth of the twins is not stated. The relation of syphilis to monsters in general is not definite, and as far as we have been able to find, in no previous pygopagi or in their progenitors is the existence of this disease recorded. The cause of death

33. Playfair, W. S.: Conjoined Twins, Tr. Obst. Soc. Lon. **32**:265-266, 1880.

34. Leonhardt, cited by Williams, J. W.: Obstetrics, ed. 5, New York and London, D. Appleton & Co., 1924, p. 413.

35. De Lee, J. B.: The Principles and Practice of Obstetrics, ed. 3, Philadelphia and London, W. B. Saunders Company, 1921, p. 555.

36. De Lee (footnote 35, p. 479).

37. Baudouin (footnote 43, first reference) says that double monsters are more common in this part of the world than in any other. When Barnum wanted double monsters for his side show he sought them in Bohemia, Austria, Hungary and the surrounding Slavic states.

of the mother of the Blazek twins, at the age of 65, is unknown. In 1922, the father was 82 years old and well.

Childhood.—At birth, Rosa and Josepha were healthy and normal except for their union posteriorly, in the region of the buttocks. For the first month of their life, the mother did not trouble to nurse them, for she had been told by the midwife that they would not live. Thereafter, on the advice of a physician, she did nurse them, weaning them when they were 2 years old. Their development was normal and independent. Both began to talk at the age of 2, and to walk at 4. They could run, jump, dance and even climb trees. About this time, they both had measles, their sole simultaneous illness. When they were 8 years old, Josepha alone had diphtheria. Although she had a high fever and delirium, her sister Rosa remained perfectly well. At 12 years, following a fright, Josepha alone had chorea. This attack lasted thirteen weeks, but the only effect on Rosa was the discomfort of confinement to bed.

Adolescence.—Both sisters began to menstruate simultaneously a month before their fourteenth birthday. Their periods occurred regularly and simultaneously thereafter, every four weeks. Both had dysmenorrhea, the pain being independent and referred to the abdominal and sacral regions. When, at the age of 14, Josepha suffered a relapse of her chorea, the menses of both sisters stopped for a few months. For four years, Rosa had a colitis with diarrhea, and Josepha's bowel movements remained normal during the entire period. Since there was a common rectum, the formed stools of Josepha were thus intermixed with the loose ones of Rosa. In temperaments, thoughts and mentalities, they were entirely different. Rosa liked sour things, and Josepha liked sweets; Rosa had sex desire, Josepha had none; Rosa was much more intelligent, although the mentalities of both were somewhat below normal. They both realized that the death of the one of them would be followed by that of the other.

When they were 25 years old, Schaeffer-Stuckert³⁸ noted the presence of all the third molar teeth in Rosa, but only the upper third molars in Josepha. He was not sure whether the latter's other molars had not yet erupted, or had already been lost.

In 1906, when they were 28 years old, Kukula³⁹ of Prague removed a stone the size of a hen's egg from the bladder of Rosa by litholapaxy. The demonstration, at necropsy, of a stricture just proximal to a polyp in the left ureter of Rosa, is mute evidence of the passage of a renal calculus which may have been the beginning of this bladder stone. Four years after the bladder operation, Rosa had intercourse with her manager, and, astounding though it may seem, gave birth to a boy, the only recorded pregnancy in a joined twin. No physician was present during the delivery, so that its mechanism is not known. Although both of the sisters had milk in the breasts, the child was given to a wet nurse for the sake of convenience. In 1922, this son was 12 years old, perfectly well and normal.

Antemortem Examinations.—The Blazek twins began to capitalize their physical union quite early, and were shown in side shows and clinics for

38. Schaeffer-Stuckert: Die Zähne der Pygopagen Rosa-Josepha Blazek, Deutsche zahnärztl. Wchnschr., Berlin 6:281-283, 1903.

39. Kukula, V.: Report of Bladder Operation on Blazek Twins, Lancet 1:345, 1906.

practically the whole of their lives. They were first examined by Breisky⁴⁰ when they were 6 months old. He examined their general condition and their physical union. He noted an asymmetry in their heads which he attributed to intra-uterine molding. This was found again twenty-five years later when Henneberg and Steltzner⁴¹ determined their physiognomonic and cranial indexes as a part of the most exhaustive study of the Blazek twins recorded. Marchand⁴² examined the twins in 1881 when they were 3 years old. In 1891, Baudouin,⁴³ Collineau⁴⁴ and Fauvelle⁴⁵ examined them. In 1906 they were examined by Kukula.³⁹ In 1910, Truneczek⁴⁶ reported the confinement of Rosa, and Basch⁴⁷ studied the milk secretion of the twins. Schauta⁴⁸ saw them in the same year, and one year later they were examined by Villapadierna.⁴⁹ Hübner,⁵ in 1911, included the twins in his review of the literature on the general subject of anomalies of development. Their last illness was reported by Breakstone⁵⁰

40. Breisky, A.: Die zusammengewachsenen Zwillings Rosa-Josepha Blazek aus Skreychov. We have been unable to confirm this reference cited by Hübner (footnote 3).

41. Henneberg, R., and Steltzner, H.: Ueber das psychische und somatische Verhalten der Pygopagen Rosa und Josepha, Berl. klin. Wchnschr. **40**:798-801 and 829-833, 1903.

42. Marchand, F.: Die böhemischen Schwestern Rosalia und Josepha, Breslauer ärztl. Ztschr. **3**:237-240, 1881; abstr., Zentralbl. f. Gynäk. **5**:614, 1881; Missbildungen, Real-Encycl. d. ges. Heilk. **9**:131, 1881; abstr., Zentralbl. f. Gynäk. **5**:612, 1881.

43. Baudouin, M.: Tératologie: Les soeurs Rosa-Josépha Blazek, Semaine méd. **30**:230-232, 1910; originally published in same journal **11**:293-295, 1891. Other reports of lesser importance by the same author are: Le monstres doubles opérables, Rev. scient. **1**:73-78, 1893; Le monstres doubles autositaires opérés, et opérables, Rev. de chir. **25**:513-577, 1902; Le mariage des monstres doubles, Gaz. méd. de Paris **2**:57, 1902; Séparation chirurgicale de deux sujets composant le monstre double Pygopage Rosa-Josépha Blazek, Bull. et mém. Soc. d'anthrop. de Par. **7**:222, 1906; La vie des monstres doubles: la croissance de Rosa-Josépha pygopage de Bohême, Aesculape **1**:66-68, 1911; La mariage des monstres doubles, ibid. **1**:104-106, 1912.

44. Collineau, D. A.: Tératologie; Rosa-Josepha, Rev. mens de l'École d'anthrop. de Par. **1**:377-378, 1891.

45. Fauvelle: Rosa-Josepha, Rev. mens de l'École d'anthrop. de Par. **1**:378-380, 1891.

46. Truneczek, C.: L'accouchement d'pygopage Rosa-Josepha Blazek, Semaine méd. **30**:229-230, 1910; Brit. M. J. **1**:1313, 1910.

47. Basch, K.: Ueber experimentelle Milchauslösung und ueber das Verhalten der Milchabsonderung bei die zusammengewachsenen Schwestern Blazek, Deutsche med. Wchnschr. **36**:987-990, 1910.

48. Schauta, F.: Die Pygopagenschwestern Blazek, Gynäk. Rundschau **4**:437-445, 1910.

49. Villapadierna, E. M.: Las hermanas Blazek, An. Acad. de obst. (etc.) **4**:401-411, 1911.

50. Breakstone, B. H.: Last Illness of Blazek Twins, Illinois M. J. **42**:123-130, 1922.

in 1922. Other observations of lesser importance are by Playfair,⁵¹ Bertillion,⁵² Delineau,⁵³ Chapot-Prévost,⁵⁴ Schaeffer-Stuckert,⁵⁵ Bilhaut,⁵⁶ Toussaint,⁵⁷ Struve⁵⁸ and Bland-Sutton,⁵⁹ and in reviews and editorials.⁶⁰

It is from this rather extensive literature that the following description is taken.⁶⁰

Rosa and Josepha Blazek were united at the posterior inferior part of the pelvis and sacrum (figs. 1 and 2). Rosa, the thinner, taller and younger looking was on the left side, Josepha on the right. The right leg of Rosa and the left leg of Josepha were adjacent and ventrally placed. The other two legs were placed dorsally and externally. Their vertebral columns were not parallel, but formed a V, the apex of which corresponded to the top of their union. In addition, their spinal columns were rotated through an angle of 45 degrees, so that the right side of Rosa and the left side of Josepha were closer to each other than the left side of Rosa and the right of Josepha, their inside shoulders forming an angle of 90 degrees with each other. Their heads were tilted inward a little so that they faced in the same direction. They were able, by turning their heads and vertebral columns, to look at each other and even to kiss each other. To allow erect carriage, there was a compensatory lumbar lordosis in both sisters. Both had funnel-shaped chests.

Their adjacent lower extremities were also not parallel but formed an inverted V with its apex corresponding to the lowest part of their union. Thus the sisters leaned against each other, somewhat in the form of an X. The union of their soft parts began at the level of the ninth thoracic vertebra (Hübner), and its circumference was about 94 cm. When standing, the

51. Playfair, W. S.: Pygopagus Twins, Tr. Obst. Soc. Lond. **22**:265, 1881; Lancet **1**:15, 1881.

52. Bertillion, J.: Rosa-Josepha, les deux soeurs tchèques, Nature **12**:293-294, 1884.

53. Delineau: Rosa-Josepha, Clinique, Paris **2**:205-208, 1891; abst., Communiqué à la Soc. Méd. Chir. des Prat. de France (Discussion), July 10, 1891, cited by Hübner (footnote 3).

54. Chapot-Prévost: Chirurgie des Tératopages, Gaz. méd. de Paris **1**:225-227, 305-308, 321-323 and 345-349, 1901; Monatschr. f. orthop. Chir. (etc.) **8**:16, 1901.

55. Bilhaut, M.: Rosa-Josepha, Ann. de chir. et d'orthop. **23**:225-235, 1910.

56. Toussaint, L.: Sensations de pygopages, Chron. méd. **17**:643-646, 1910.

57. Struve, K.: Die lebenden Doppelmissbildungen, Königsberg, O. Kummel, 1912.

58. Bland-Sutton, Sir J.: Rosa-Josepha Blazek, the Bohemian Twins, Lancet **1**:772, 1922.

59. Reviews: Un monstre pygopage, les soeurs Rosa-Josepha, Rev. scient. **48**:92-94, 1891; Rosa-Josepha, Relation Médicale, Tiré à 'port **8**:11, 1891, cited by Baudouin (footnote 43); Rosa-Josepha, Am. Naturalist **25**:891-894, 1891.

60. The only published picture showing the Blazek twins naked in the region of their union may be found in the article by Breakstone (footnote 50). Pictures of the twins dressed are in the feature section of the Chicago Herald and Examiner, Sunday, April 16, 1922; in the articles by Bertillion (footnote 52), by Chapot-Prévost (footnote 54), by Toussaint (footnote 56), by Baudouin (footnote 43, sixth reference); in the Leipz. Illus. Zeitung, 1892, no. 2576; and in Gould, G. M., and Pyle, W. L.: Anomalies and Curiosities of Medicine, Philadelphia, W. B. Saunders Company, 1897.

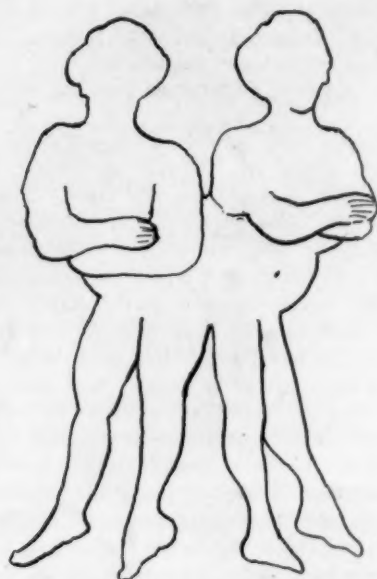


Fig. 1.—From a photograph of the Blazek twins in Dr. Breakstone's article. Josepha is on the right and Rosa on the left. This and figures 2 and 4 illustrate, in a general way, the character of the union in all pygopagus twins.

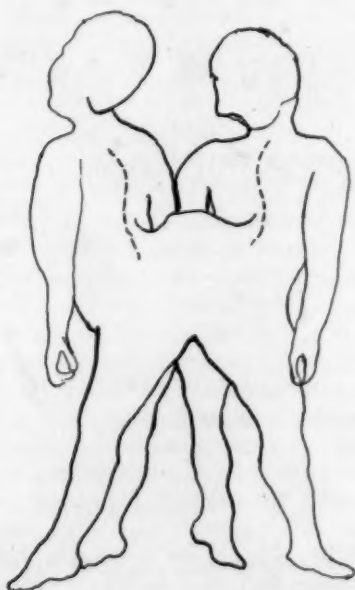


Fig. 2.—Dorsal view of the Blazek twins, from a photograph in Dr. Breakstones' article.

distance between their medial jugular fossae was 48 cm., between their nose tips 50 cm., between their seventh cervical spines 39 cm., between their inner shoulders 20 cm., and their outer shoulders 70 cm., between their inner anterior superior iliac spines 20.5 cm., and between their outer anterior superior iliac spines 36.5 cm. The interspinous distance was 20 cm. in Rosa, and 21 cm. in Josepha. The intertrochanteric distance was 28 cm. in the former and 27 in the latter. Rosa was 144 cm. long and Josepha 2 cm. shorter. Their combined weight in 1910 was 85 Kg. Josepha's left leg was 5 cm. shorter than her right, so that when standing, only the ball of her left foot touched the ground. Figure 3, showing the projection on the floor of important landmarks, indicates the position of the sisters when standing. In walking they would place the ventral pair of legs forward simultaneously, or alternately, and then bring up their dorsal pair. When one walked directly forward the other naturally would have to walk backward. They could stand on two, three or four legs and each could swing the other off the ground by the buttocks. As far as could be determined by palpation and percussion, there was no *situ inversus* and the heart, lungs, liver,⁶¹ stomach and colon were normally placed.

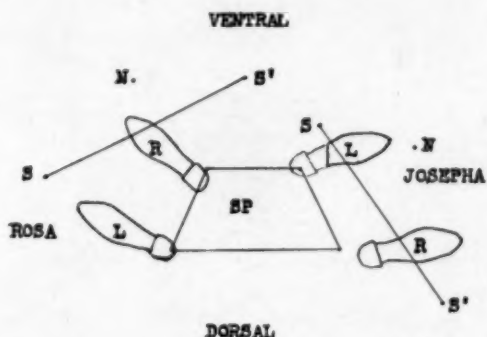


Fig. 3.—The projection on the ground of bony landmarks of the Blazek twins when standing (from Henneberg and Steltzner); SP indicates a trapezoid formed by lines connecting the anterior superior spines of the ilia; SS', lines through the shoulders; N, tip of the nose; R, right foot; L, left foot; the dotted portion of Josepha's left foot corresponds to the portion that does not touch the ground.

The greatest degree of union was apparent in the perineal region. With the sisters lying down in their usual manner, that is, Rosa on her left side and Josepha on her right, and with the knees and thighs flexed, the common genital region was visible (fig. 4). There was a common anus (fig. 4, 21) placed in a common anal groove formed by the two buttocks on which the sisters lay. In a common isosceles triangular area with its apex at the anus and the base formed by a line connecting the two montes veneris, the common genito-urinary orifices were in a line corresponding to the perpendicular bisector of the triangle. These orifices were normally placed with respect to each other but were rotated through a 90 degree angle with respect to the montes veneris. There were three labia majora (fig. 4, 17) parallel, more

61. At the postmortem examination, the liver of Rosa was found reversed, its major portion being on the left.

or less, to the sides of this triangle. One of them, that parallel to the base, was 14 cm. in length and 4 cm. longer than either of the other two; probably, it was the fusion of two labia. Beneath it could be felt the adjacent tubera ischii of the sisters (shown by dotted lines in fig. 4), which were fused in a bony mass. Below this labium majorum, two labia minora came together to form a common well developed clitoris (fig. 4, 18). There was a common urethral orifice (fig. 4, 19) just below the clitoris. Its transverse diameter was greater than its vertical, and it was partially hidden by an overhanging flap of mucous membrane (fig. 4, 10). Truncceck believed that this indicated a fusion of two separate urethrae, the flap being the remnant of the septum which once had separated them. He suggested the schema shown in figure 5 to explain the mechanism of the fusion of the genito-urinary systems. In

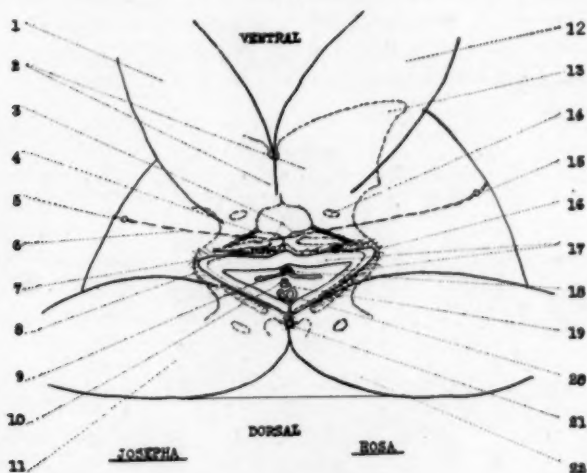


Fig. 4.—The external genitalia of the Blazek twins (modified from Henneberg and Steltzner). The probable relations of the bony pelvis are indicated by the dotted lines; for the sake of clarity, only the right iliac bone of Rosa is filled in; the dashed lines (6, 7) represent incisions made at necropsy. 1, indicates the left leg of Josepha; 2, the left ilium of Josepha and the right of Rosa, showing the probable nature of their union; 3, the left ischium of Josepha and the right of Rosa, united; 4, the ascending ramus of Josepha's left ischium, where it was sawed through at necropsy—the places in which the other bones were sawed through are indicated by three other double wavy lines; when these four places were sawed through it was possible to throw the ventral extremities upward, as mentioned in the text, and thus to enter the pelvic cavity; 5, umbilicus of Josepha; 6, horizontal incision connecting the two mid-line incisions made at necropsy; 7, vertical incision, extending from the horizontal incision to the labium majorum; 8, pubic symphysis of Josepha; 9, labia minora; 10, mucous membrane flap, overhanging urethral orifice; 11, right leg of Josepha; 12, right leg of Rosa; 13, anterior superior spine of the right ilium of Rosa; 14, right acetabulum of Rosa—the other three acetabula are indicated, but not labeled; 15, umbilicus of Rosa; 16, pubic symphysis of Rosa; 17, labia majora; 18, common clitoris; 19, common urethral orifice; 20, common vaginal orifice, divided by a septum; 21, common anal orifice; 22, left leg of Rosa.

normal twins who are placed back to back, the external genito-urinary orifices are placed as figure 5, *A*. If the lines passing through the genito-urinary orifices of each be rotated through an angle of 90 degrees, with the midpoint as a pivot, the arrangement of these orifices will be as indicated in figure 5, *B*. The latter diagram corresponds to the condition prevailing in pygopagus twins. By passing sounds through the urethral opening, Trunccek found that "the urethra was common for only 3 cm., beyond which it divided into two short canals, each having its own sphincter and leading into two separate bladders. By a cystoscopic examination, it was found that in Josepha the ureters entered the bladder irregularly. They entered a little to the right of the median line and were placed one above the other less than a centimeter apart. In Rosa, the ureteral orifices were symmetrically placed in the bladder about 1.5 cm. apart.⁶² Four years after her litholapaxy, her bladder showed the signs of a chronic inflammation" (translated).

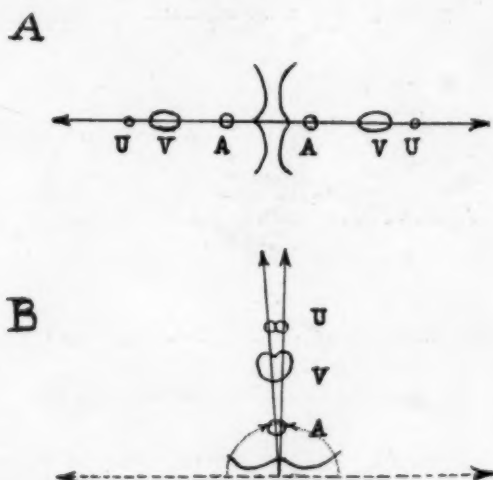


Fig. 5.—Possible mechanism involved in the union of the genito-urinary orifices of pygopagi (from Baudouin). Section *A* shows the relation of the genito-urinary orifices in normal twins, placed back to back; section *B*, the relation of these orifices after rotation occurs as indicated by the arrows—these relations exist in all pygopagi, to a greater or less extent. In the sections, *A*, indicates the anal orifice; *V*, the vaginal orifice; *U*, the urethral orifice.

Beneath the common urethral orifice, a common, asymmetric, heart-shaped vaginal orifice (fig. 4, 20) was divided into two parts by a longitudinal septum 0.75 cm. thick. Rudimentary hymens were present in each half. There were two vaginal canals, and two uteri of normal size and position except for a sharp antelexion of Josepha's uterus.

The common anal opening was separated from the vaginal introitus by a narrow extent of perineum. There was a common rectum for 5 cm., beyond which it was divided proximally in two by a septum which arose from the posterior wall of the rectum. Rosa's sigmoid was placed a few centimeters higher than that of Josepha.

62. These observations on the positions of the ureteral orifices were confirmed, for the most part, by the postmortem examination (fig. 8).

The exact nature of the bony union, to be discussed later, is not known, as a clear roentgenogram was never made. However, by physical examination, it was known that Rosa's pubic symphysis was symmetrically formed and that her pubic and ischiatic bones were well developed. There was a flattening in her left acetabular region and a similar flattening in Josepha's right acetabular region, due perhaps to a greater weight carried by the corresponding legs. In Josepha, on the other hand, the symphysis pubis was asymmetric, its left part being much thinner than the right. Both rami of her pubic bones were somewhat flattened toward the superior strait of the pelvis. Her left ischium was considerably thinned. Beneath the common urogenital region, the four tubera ischii were easily palpable, and just medial to these the ascending rami of the adjacent ischii were united in a bony mass (fig. 6, 4 and 6). There were four well formed iliac bones the adjacent posterior portions of which were more or less fused. Baudouin believed (and his opinion was confirmed at the necropsy) that they had one large bony pelvis, and Henneberg and Steltzner believed that their pelvic girdles were separate.

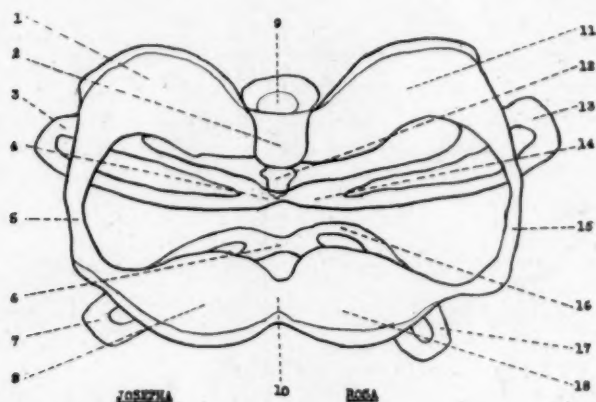


Fig. 6.—Diagram of the common bony pelvis of the Blazek twins, showing the probable nature of the bony union, viewed from above downward; 1, indicates the right ilium of Josepha; 2, the common sacrum; 3, the descending ramus of the right pubic bone of Josepha; 4, the union of the adjacent dorsal pair of ischia; 5, the pubic symphysis of Josepha; 6, the union of the adjacent ventral pair of ischia; 7, the descending ramus of the left pubic bone of Josepha; 8, the left ilium of Josepha; 9, the fifth lumbar vertebra; 10, the union of the ventral pair of ilia; 11, the left ilium of Rosa; 12, the common coccyx; 13, the descending ramus of the left pubic bone of Rosa; 14, the tuberosity of the left ischium of Rosa; 15, the pubic symphysis of Rosa; 16, the tuberosity of the right ischium of Rosa; 17, the horizontal ramus of the right pubic bone of Rosa; 18, the right ilium of Rosa.

Many who examined these twins thought that their bony union closely simulated that in the pygopagus studied by Marchand and by Adolph. We quote here from Marchand's account of the bony union.

"There is a common coccyx and sacrum (fig. 7). The spine of the first sacral vertebra is divided, each half being directed toward a separate fifth lumbar vertebra in each twin. The left ilium of the twin on the left (fig. 7. 4)

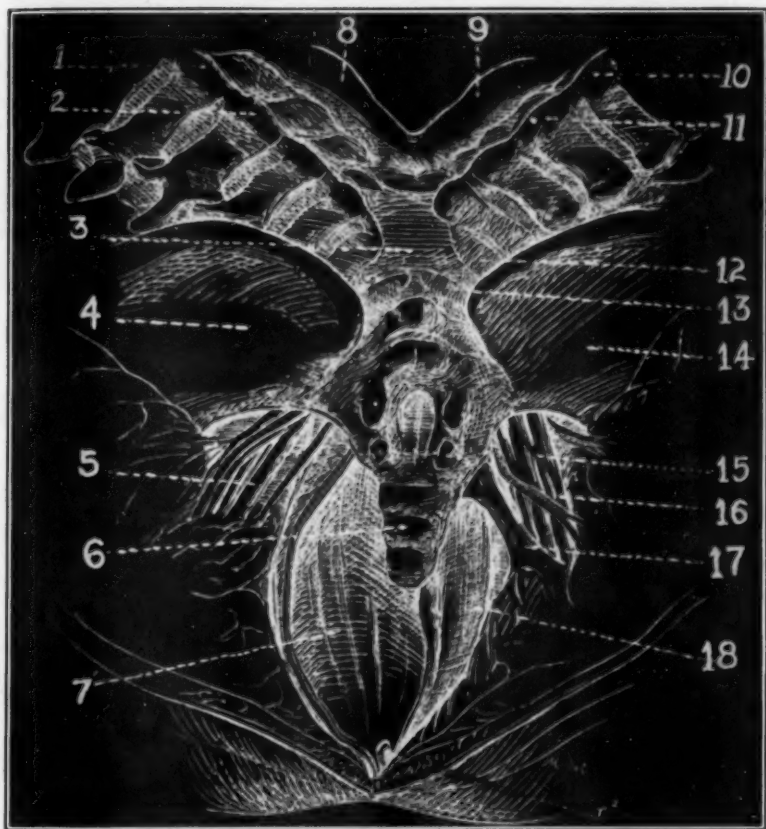


Fig. 7.—Dorsal view of the vertebral columns and surrounding parts in twins studied by Marchand (reproduced from Marchand); the common buttock has been opened from behind so that both recta are visible; 1 indicates the vertebral column of left body; 2, the third lumbar spine; 3, the fibrous membrane covering the common spinal canal; 4, the left ilium of the left body, joining the common sacrum; 5, the left sciatic nerve of the left body; 6, the coccyx; 7, the rectum of the left body; 8, the right ilium of the left body—this and the left ilium of the right body unite with each other and with the union of their vertebral columns; 9, the left ilium of the right body; 10, the vertebral column of the right body; 11, the third lumbar spine; 12, the first sacral vertebra; 13, the second sacral vertebra; 14, the right ilium of the right body; 15, the right sciatic nerve of the right body; 16, the ischiatic artery; 17, the sacrotuberous ligament of the right body; 18, the rectum of the right body.

and the right ilium of the twin on the right (fig. 7, 14) are connected to the common sacrum. Their other ilia, i. e., the right of the one on the left side (fig. 7, 8) and the left of the one on the right side (fig. 7, 9) are united to each other by a cartilaginous union above and a fibrous one below. They do not attach to the sacrum at all, but to the respective processes of their lumbar vertebrae together with which they form the bony anterior wall of the spinal canal" (translated). In Helena-Judith and in Tynberg's pygopagus, there was also one common sacrum from the second sacral vertebra and from the third sacral vertebra, respectively, caudad.

In the Blazek twins, according to Henneberg and Steltzner, from the second lumbar vertebra caudad there was a common spinal column, sacrum and coccyx. According to Schauta, however, the union in the Blazek sisters involved only the medial halves of the sacra and coccyges, a condition which prevailed in Chrissie-Millie,¹⁸ in the pygopagi studied by Wolff in whom "only one-half of the pelves were united, from the upper margin to the coccyx" (translated), and in the twins studied by Barkow, in whom the union between the halves of the sacra was ligamentous.

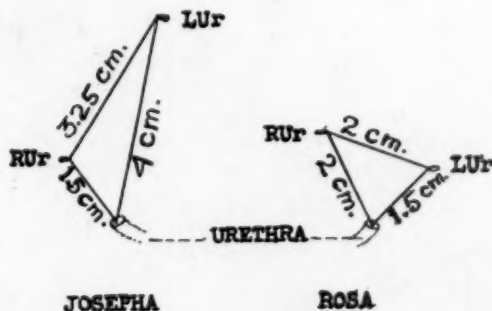


Fig. 8.—The relations of the urethral and ureteral orifices of the urinary bladders of the Blazek twins (actual size); RUR indicates the right ureteral orifice; LUr, the left ureteral orifice.

In the Samar twins, the union was fibrous and did not involve the bones of the pelvis; in Treyling's pygopagi and in the Hilton twins the union involved the coccyges only; in the twins reported by Pare¹ (born in 1475), Von Normand, Molitor, Joly and Peyrat, Grosse, Achren and Géniaux, the union involved at least the sacrum. No mention is made of a bony union in those twins reported by Ballantyne (the Biddenden Maids), by Pare¹ (born in 1486) and by Carmicheal.

Whether or not there was a common cauda equina or common spinal canal in the Blazek twins is not known definitely. Marchand and Barkow demonstrated a union of the inferior portions of the spinal cords in the respective pygopagus twins they examined. That a similar condition prevailed in Millie-Chrissie and in Lassen-Elaoussin (reported by Géniaux) is probable, because stimuli applied to the lower extremity of one twin were felt by the other also. In Tynberg's pygopagus there was a communication between the dural sacs of the twins, but the spinal cords were not united. Henneberg and Steltzner, on the basis of their examination of the nervous system of the Blazek sisters, believed that there was no extensive connection of their spinal cords, for sensation in these twins was entirely separate except for a common area which

was about 7 cm. wide, at the back of their union and which gradually narrowed to 1 cm. in width anteriorly. Common sensibility was present also in the rectum, vaginae, urethra and clitoris. Thus when Rosa had intercourse with her manager, Josepha admitted that she also had libido. They both felt the passage of urine through their common urethra. However, the desire to urinate was separate for they had separate bladders which explains also why Rosa alone felt pain during her bladder operation. During the labor of Rosa, Josepha too felt pain, but this may have been due to the stretching of their common perineum or to pressure by the child on Josepha's cervix. That the first of these did occur is evident from a mucosal tear which extended to Josepha's vagina, following the delivery of Rosa. Although there was separate innervation of the sphincter ani, the desire to defecate was felt by both simultaneously, and an enema acted on both of them if the tube was inserted for a distance of less than 5 cm. If it was inserted farther, the action was independent, for proximal to this point, the recta with their innervations were separate. Sensation in the lateral walls of the vaginae, in the labia minora, in the lower labia majora and in the vulvae was independent. Moreover, the superficial, tendon and eye reflexes of the Blazek twins were normal and independent.

Whereas the degree of sensitivity in all other places was normal, in the region of common sensibility it was approximately halved, so that, as Baudouin remarks, their husband would require double potency to satisfy them sexually. A similar reduction in sensitivity was present in the common penis of Lassen-Elaoussin, so that they had never had an erection or the desire for one. Henneberg and Steltzner attempt to explain this reduction in sensitivity on the division between the two persons of the normal number of nerve endings to the common area.

In the twins studied by Marchand and in those studied by Torkos (Judith-Helena, the Hungarian sisters) there were anastomoses between the inferior aortas and venae cavae. In Tynberg's pygopagus and in the Blazek sisters, however, there were no such extensive anastomoses. Not only were the temperatures and the radial pulse rates of the Blazek twins different, but also their dorsalis pedis pulses were synchronous with their respective radial pulses. Moreover, in the postmortem examination of the body, evidence of syphilis was found in Rosa only. Altogether, these facts indicate the absence of any extensive vascular connection in the twins. However, that there was some interchange of blood may be inferred from the simultaneous onset and occurrence of menstruation in the sisters; from the temporary cessation of the menses of both sisters when Josepha alone had chorea; from the pigmentation of the linea alba and of the nipples and from the enlargement of the thyroid glands of both sisters during Rosa's pregnancy; from the cessation of Josepha's menses during the last two months of Rosa's pregnancy; and from the presence of milk in the breasts of both. Basch, who analyzed the milk, stated that the milk of Josepha, the nonpuerperal, was richer and more abundant than that of her sister. He explained these phenomena on the basis of the passage of a hormone from the circulation of one sister into that of the other at the site of union. This would not explain, however, why Josepha menstruated up to the eighth month of Rosa's pregnancy.

Henneberg and Steltzner gave one of the sisters potassium iodide by mouth and within one hour found it in equal concentrations in the salivas of both of them, demonstrating conclusively that there was some exchange of blood. This exchange could not have been extensive, for when one of the sisters

held her breath, she alone had the signs of discomfort and suffocation. The final evidence of a vascular connection, is the cholemic coma which developed in Rosa, as well as in Josepha, following an acute yellow atrophy of the liver (demonstrated at necropsy) in the latter.⁶³

Final Illness.—From 1910 to 1922, there is apparently no record of the health of the Blazek twins. In 1922, Rosa was taken ill with influenza. Three weeks later while she was recovering from this attack, her sister Josepha had an attack simulating appendicitis, followed by jaundice. Dr. Breakstone of Chicago, who attended them, made a clinical diagnosis of appendicitis or cholecystitis. When they entered the hospital, Josepha was very ill, while Rosa was feeling well. Their common bowel movements contained Josepha's slate-colored stool mixed with Rosa's normal one. The urine was normal, not even bile being present. Josepha's blood had a hemoglobin content of 80 per cent, 4,800,000 red cells and 8,000 white cells. Rosa's blood had a hemoglobin content of 80 per cent, 5,000,000 red cells and 7,000 white cells. Nothing grew on culture mediums to which blood from Josepha was added. Josepha's temperature was 98.8 F., that of Rosa 97.8 F. The former's pulse rate was 94 and the latter's 90.

Josepha's condition grew worse. The temperatures and pulse rates of both sisters rose, those of Josepha being continually slightly higher than those of her sister. When it became evident that Josepha's illness was critical the question arose of separating the twins surgically with the possibility of saving Rosa's life. Before any such steps were taken, however, coma attributed to cholemia developed in Josepha. Within twenty-four hours the same condition developed in Rosa. Finally both sisters developed a terminal bronchopneumonia and on March 30, 1922, five days after their entrance into the hospital, Josepha died. The death of Rosa followed twelve minutes later.⁶⁴ They died at the West End Hospital in Chicago, at the age of 43.

Postmortem Observations.—Necropsy was performed by one of us (E. R. L.) assisted by H. A. Oberhelman, because of legal questions regarding which of the twins had given birth to the child.⁶⁵ It was performed on April 2, 1922, three days after death, and it was hampered by lack of time, the poor facilities in the garage of an undertaker's establishment where it was performed, and stipulations as to what should be examined.

The external examination confirmed essentially those conditions reported during life. "These are the bodies of two white women joined at the left hip and buttock of one with the right hip and buttock of the other . . . The circumference of the union between the two trunks is 100.5 cm., its vertical diameter 32 cm. and its horizontal diameter 12 cm. The outer breast of each body is pendulous, the inner flat. The nipples are all flat. There are striae gravidarum of the abdomen of the left body (Rosa), but none of the right (Josepha). The feet and hands are small and alike. The right ulna of the right body is 22 cm. long, and that of the left body is 1 cm. shorter. The two ventral extremities are a little shorter than the dorsal . . . There is no

63. In the case of Helena and Judith in whom anastomoses of the inferior aortas and venae cavae were demonstrated post mortem, when one had malaria, the other remained well.

64. The Tynberg twins died eight hours apart. This is the longest recorded interval between the deaths of pygopagus twins.

65. Dr. J. H. M. Otradovec assisted with the record of the postmortem examination.

striking resemblance of the two faces, the right being fuller. The skin of each body is yellowish green. Both bodies are embalmed and have a strong odor of formaldehyde."

Right Body (Josepha).—On internal examination of Josepha's body, the brain, which weighed 1,275 Gm., had an area of softening 5 mm. in diameter in the pons varolii. The thyroid gland weighed 33 Gm. and was normal except that its right lobe was larger than its left.

"The thorax seems normally developed as regards cartilages, ribs, and sternum. The right side of the thorax is small; the left is of normal size. There is a large curve of the spine to the left, its greatest departure from the midline at the level of the sixth thoracic vertebra. There is a compensatory curve to the right, and its greatest departure from the midline is at the second lumbar vertebra. From here down, the spine curves to the left again, so that it almost meets the spine of the other body at the common union of the trunks."

The right lung weighed 435 Gm. and had two accessory fissures—a vertical one in its upper lobe and a horizontal one in its middle lobe. The left lung weighed 330 Gm. and was normally lobated. Its fissure was obliterated in most of its extent by fibrous adhesions. Any gross changes which may have been present in the lungs were masked by the embalming fluid.

The heart weighed about 250 Gm. Its chambers were small for the size of the trunk, but it was otherwise normal. The pulmonary artery was short, being 12 mm. from root to mouth. There was a slight hyperplasia of the tracheo-bronchial lymph glands.

The subcutaneous fat exposed by a midline incision through the abdominal wall had a maximum thickness of 3.7 cm. The bowel and great omentum were normally free. The mesenteric and omental lymph glands were slightly hyperplastic and streaked black. "The lower margin of the liver is above the costal margin. . . . The diaphragm is at the level of the fifth rib on each side. . . . That part of the vena cava in the notch behind the liver is entirely surrounded by liver tissue." There were fatty changes present in the lining of the aorta.

"The liver is small being 16.5 by 10.5 by 11 cm. Its surface is nodular from pale yellow green projections. Inside the liver there are yellowish green places so that one-fourth of each of the two large surfaces made by cutting the liver has such color. In general, this liver has the appearance of acute yellow atrophy." The liver weighed only 710 Gm. In the neck of the gall-bladder was a solitary oval, dark green, easily cut gallstone, 2 cm. long and 1.2 cm. in diameter. The spleen weighed 108 Gm., and was bound by fibrous adhesions to the diaphragm, but otherwise was unchanged. The stomach, esophagus, intestines and pancreas, were grossly normal. The suprarenal glands were unchanged except that the right was lower than normal. The left kidney was normal in position and appearance. It weighed 150 Gm. The right kidney lay low down in the pelvis and will be described with the pelvic organs. There was no anomaly about the blood supply to either kidney.

Left Body (Rosa).—The brain weighed 1,225 Gm. and was grossly normal. The thyroid gland weighed 38 Gm. and contained a colloid cyst, 3 mm. in diameter in its left lobe.

"The costal cartilages are soft. There is a similar curving of the spine and a similar narrowing of the left chest, as in the right body." The lungs were grossly normal as far as could be determined, except for two shallow accessory fissures of the left lung. The right lung weighed 443 Gm. and the left 433 Gm.

The heart, which was in its normal position, weighed 261 Gm., and was grossly unaltered. The pulmonary artery and its branches were of normal length. The arch of the aorta was thickened, and the lining of the proximal portion of the thoracic aorta roughened, wrinkled and thickened, with the appearance of syphilitic aortitis.

The subcutaneous fat exposed by a midline incision through the abdominal wall had a maximum thickness of 3 cm. The diaphragm was at the level of the sixth rib on the left and at the sixth interspace on the right. "There are no adhesions about the abdominal viscera. The viscera are all placed in their normal positions except the liver which is reversed so that its major portion is on the left.⁶⁶ Its surface is mottled with yellow but is not nodular like that of the other body." This liver weighed 733 Gm. and grossly had the appearance of a liver with acute fatty changes.

The spleen was on the left side of the body, was acutely hyperplastic and weighed 210 Gm. The stomach and intestines were grossly normal. The right kidney was slightly enlarged, but otherwise normal. It weighed 183 Gm. The left kidney was not located until the common pelvis was opened.

The common pelvic cavity was exposed from below. The midline incisions of both trunks were first connected by an incision which passed over the front of the union (fig. 4, 6) just above the labia majora. This incision was then continued vertically down (fig. 4, 7) to the labium majorum, thus exposing the horizontal and ascending rami of the ischia which were then sawed through in four places (fig. 4, 4). This allowed the ventral extremities which remained connected to each other by the union of their respective ischia to be turned upward, until they lay over the faces of their respective bodies. The common pelvic cavity was thus brought into view.

There was no connection between the peritoneal cavity of one body with that of the other in the pelvis or elsewhere. There was no connection between the aortas or inferior venae cavae, and such vascular anastomoses as did exist must have involved the iliac vessels or their branches. There was one common bony pelvis.⁶⁷ The exact arrangement of the bony framework was not studied because of the conditions attending the necropsy.

One may, nevertheless, draw a fairly accurate conception of the nature of the bony union in the Blazek twins. Figure 6 illustrates our conception of this union as viewed from above down. Figure 4 presents an inferior view of this union depicted in dotted lines. The union of the two dorsal ilia to the common sacrum was probably of the same type as that described by Marchand in the twins studied by him. The union of the ventral ilia must of necessity have been different, for the Blazek twins possessed a common pelvis, whereas in the twins studied by Marchand, the ventral ilia were united not only to each other, but also to the transverse processes of the second lumbar vertebrae, thus forming two separate pelvic girdles. The ventral pair of ischia (fig. 6, 6) in the Blazek twins were doubtless united, as were the

66. No *situ inversus* was present in the pygopagus twins studied by Treyling, Torkos, Barkow and Marchand. In Tynberg's pygopagus, however, there was a *situ inversus* of the liver of the left body, similar to that found in the Blazek twins. Achren states that in the twins studied by him, the heart of the right twin was on the right side.

67. In Helena-Judith, and in Tynberg's pygopagus, there was also a common pelvis, and, likewise, there was no communication between the peritoneal cavities in either of these pairs of twins.

dorsal pair (fig. 6, 4). However, there was probably no union of the ventral pair to the dorsal pair, for the sawing through the rami of the ventral pair of ischia alone allowed the ventral extremities to be thrown upward as described.

"There is a moderate amount of fat surrounding the structures low down in the pelvis. The right kidney of the right body lies against the right pelvic wall, just below its brim.⁶⁸ Its upper pole is 6 cm. below the level of the upper margin of the fundus uteri." There was a chronic diffuse nephritis with secondary contraction so that this kidney weighed only 90 Gm. "The renal pelvis resembles a dilated ureter and the calyces emptying into it are no more than 2 to 3 mm. in diameter, resembling more the tributaries to a large vein than the calyces of a normal kidney pelvis. The ureter from this kidney takes a tortuous course, encircling the outer half of the rectum and the lower part of the fundus uteri, passing forward into the urinary bladder at its normal site."

The left kidney of the left body was located only by following the ureter from the bladder upward. In the lumen of this ureter 6 cm. from its bladder opening, there was a polyp (fig. 9, 17) 1.2 cm. long and 1.5 mm. in diameter, which obstructed the lumen of the ureter almost completely. "Ten cm. above the bladder orifice, the ureter becomes dilated to a maximum circumference of 2 cm., and this for a longitudinal distance of 5 cm. Then for 1 cm. of its length, its channel is 9 mm. in circumference and immediately proximal to this it joins an irregularly dilated renal pelvis whose maximum depth is 3 cm. When the fat adherent to the kidney is separated from it, the kidney is a firm flat piece of tissue 8 cm. long, 4 cm. wide and 1.5 cm. thick. It lies against the left pelvic wall. . . . Its upper pole is 6 cm. below the level of the upper margin of the fundus uteri. There is only a small amount of kidney tissue left and this consists of multiple small cysts and fibrous tissue. This kidney, weighs only 32 Gm. . . . There is no change in the other ureter of this body or of the blood supply of either of its kidneys."

There were two urinary bladders (fig. 9, 7 and 19) and their outlets passed medially to join 1 or 2 cm. distal to each internal urethral orifice to form a common urethra (fig. 9, 8). The bladders were both normal, except for engorgement of the blood vessels about the trigone of Rosa's bladder, and for the presence in the same bladder of a submucous cyst 5 mm. in diameter, which contained a firm, brown, homogeneous substance. The linings of both bladders were greenish yellow.

Trunccek's observations on the asymmetric arrangement of the ureteral orifices were confirmed. They were placed as indicated in figure 8.

"There are two uteri (fig. 9, 4 and 14) which are normally placed with respect to the corresponding urinary bladders. The left uterus from the tip of the cervix to the top of the fundus is 13 cm. long, 9 cm. wide and 8.5 cm. broad. The right uterus is 10.5 cm. long, 10 cm. wide and 7 cm. broad. Both uteri are studded with fibroids from 1 mm. to 2.5 cm. in diameter, more numerous on their posterior surfaces. The cervix of the left uterus is 4.5 cm. long, and that of the right uterus 2 cm. long. The external os of the left cervix is slit-like, while that of the right is round." The uteri were bound together by a band of dense connective tissue and fat, and together they formed a V, the apex of which corresponded to the position of their cervixes.

68. In Marchand's twins, the left kidney in each of the bodies was displaced into the pelvis.

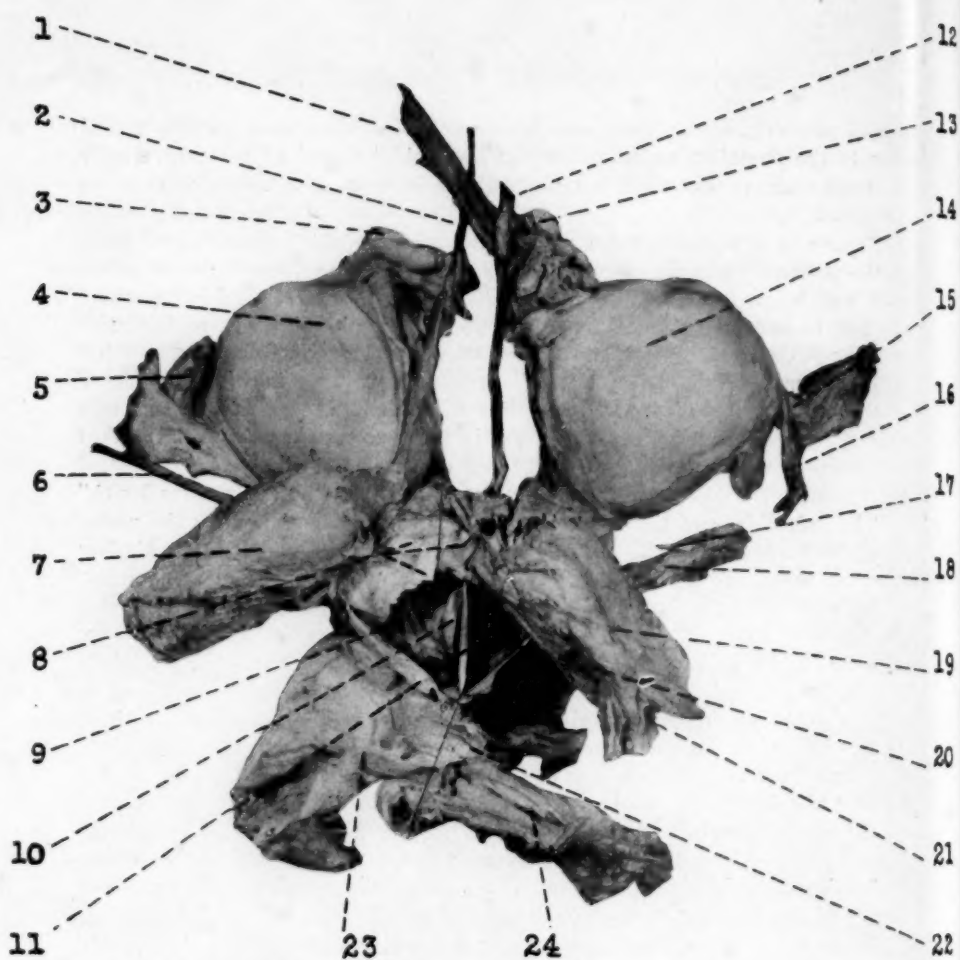


Fig. 9.—Photograph of the formalin hardened pelvic organs of the Blazek twins, ventral view. For the sake of clarity, the recta have been cut open and turned downward, with proximal parts nethermost, so that their ventral walls are visible; the urinary bladders have been tilted forward and downward; the ureters have been pulled out straight, and stitches have been used where necessary. 1, indicates the right broad ligament of Rosa, stretched out; 2, the left ureter of Josepha—its point of entrance into the bladder is clearly visible; 3, the left ovary of Josepha—the fallopian tube is ventral to it and embraces it; 4, the uterus of Josepha—the nodular elevations of this uterus as well as of the opposite one may be seen; 5, the right ovary of Josepha—a remnant of broad ligament supports it; 6, the right ureter of Josepha; 7, the urinary bladder of Josepha; 8, white tape marking the positions of the two urethrae, uniting distally to form a common urethra; 9, the vaginal canal of Josepha, narrower than that of Rosa; 10, tongue-shaped projection of vaginal septum; 11, wooden match placed in vaginal orifice to keep it distended; 12, the right ureter of Rosa; 13, the right ovary of Rosa; 14, the uterus of Rosa; 15, the left ovary of Rosa; 16, the left fallopian tube of Rosa; 17, the polyp which blocked the lumen of the ureter; 18, the left ureter of Rosa, opened to disclose the polyp; 19, the urinary bladder of Rosa; 20, the vaginal canal of Rosa; 21, the vesico-uterine pouch; 22, the septum separating the two recta—the common portion of the rectum is not visible, being hidden from view by the distended vaginal orifice; 23, the rectum of Josepha; 24, the rectum of Rosa.

There were two fallopian tubes (fig. 9, 16) and two ovaries (fig. 9, 3, 5, 13 and 15) for each of the uteri. The fallopian tubes of the left body were both thickened, kinked and somewhat clubbed, and the ovaries of this body were held to the fundus by fibrous adhesions. All four ovaries were of normal size, and each contained several cysts from 2 to 4 mm. in diameter, with brown linings and a green gelatinous content. The fallopian tubes of the right body were unchanged.

There was a partial reduplication of the vaginal canal. "When the vagina is looked into from below, the external os of the left cervix is plainly seen because the vaginal canal on this side is 3 cm. in diameter. The diameter of the right vaginal canal is 2 cm. and of the common canal 4 cm. In the lumen of the left vagina there is a tongue-shaped piece of tissue (fig. 9, 10) 3 cm. long and 0.3 cm. thick, and its base is 3 cm. long where it attaches to the septum which divides the two vaginal canals. This tongue shaped projection, when reflected upward, can be made to fit on the front wall of the common vagina, as though at one time it had formed part of the septum separating the two vaginal canals. Its distal end represents the bifurcation of the common vaginal canal which is continued distally to terminate in one common vaginal orifice."

There was a common rectum from a point 5 cm. from the common anal orifice and distally. Proximal to this point there was a well defined septum (fig. 9, 22), 4 cm. wide, which divided the common rectum into two separate recta, each continued into its respective sigmoid. Rosa's sigmoid was 4 cm. higher than that of Josepha. The lines of insertion of the rectal and vaginal septums along the rectovaginal wall, were practically identical.

Anatomic Diagnosis for Josepha.—"Acute yellow atrophy of the liver; marked generalized icterus; focal softening of the pons varolii; chronic diffuse nephritis, chronic glomerulonephritis; slight hyperplasia of the tracheobronchial lymph glands; solitary gallstone in the neck of the gallbladder; misplacement of the right kidney into the pelvis; fatty changes of the aortic lining; multiple uterine fibroids; congenitally short pulmonary artery; fibrous adhesions between the spleen and diaphragm; accessory fissures of the right lung; scoliosis of the thoracic portions of the spine with compensatory bending of the lumbar portion; hypostatic edema of the lungs; multiple small cysts of the ovaries; hyperplasia of the mesenteric lymph glands."

Anatomic Diagnosis for Rosa.—"Acute fatty changes of the liver; marked generalized icterus; acute hyperplasia of the spleen; hypostatic edema of the lungs; syphilitic aortitis; polypus-obstruction of the left ureter; chronic hydronephrosis with marked atrophy of the left kidney; compensatory hyperplasia of the right kidney; multiple small cysts of the ovaries; fibrous adhesions between the uterus and ovaries; multiple uterine fibroids; scoliosis of the thoracic portion and compensatory curve of the lumbar portion of the spine; small cyst beneath the lining of the urinary bladder; misplacement of the left kidney into the pelvis; striae gravidarum of the abdomen; syphilitic cirrhosis of the liver; hypostatic bronchopneumonia; chronic salpingitis; situ inversus of the liver."

Common Anatomic Diagnosis.—"Congenital union between the left buttock of one and the right of the other (pygopagus twins); common bony pelvis; narrowed outer chest cavities; common urethral, vaginal and anal orifices; partial reduplication of the urethral, vaginal and anal canals; slight shortening of the ventral extremities."

Microscopic Examination.—A microscopic examination was made of the lungs, liver, spleen, myocardium and aorta of each body, and of the diaphragm, pancreas and a lymph gland of the body of Josepha. The gross alterations were generally confirmed by this examination.

In the liver of Josepha there remained only about 4 per cent of normal liver tissue in a 3.5 sq. cm. section. Numerous new bile ducts were arranged more or less about the periphery of liver lobules, and within the lobules were necrotic liver cells, with many mononuclear leukocytes and dilated liver sinuses and central veins full of red blood corpuscles.

In the lungs from the same body there was an edema of the air spaces involving 50 per cent of the 3 sq. cm. in the sections. No bronchopneumonia was present in the sections studied.

The liver of Rosa was cirrhotic so that only 60 per cent of liver tissue remained in the 7 sq. cm. in the sections studied. Her lungs contained numerous red blood corpuscles in the air spaces so that in an area of 10 sq. cm., about 60 per cent of the lung tissue was so consolidated. One area of bronchopneumonia was present also.

SUMMARY

Pygopagus twins, of which only twenty-three pairs have been reported, are that class of joined twins wherein the body axes are more or less parallel and the union involves the posterior inferior parts of the trunk. There is always more or less fusion of the distal and external portions of the genito-urinary systems and always a common anus. The Blazek twins, Rosa and Josepha, are typical of this class. Of particular interest and significance with regard to the Blazek twins are the following:

1. They were the third pair of such twins to be born with two placentas and two cords (if we may believe the father), a condition which would mitigate against the theory that all joined twins are unioval.
2. They died at the age of 43, having survived longer than any other such pair of twins.
3. The necropsy is the sixth to be performed on pygopagus twins, and the second on such adult twins.
4. There was present a situ inversus of Rosa's liver, a similar condition in pygopagus twins being reported but once previously.
5. Rosa had syphilitic changes in her liver and aortic lining, while Josepha had none. The only other recorded instance of a blood borne infection existing in only one of such twins is in the sisters Helena-Judith, only one of whom had malaria.
6. There was only one common bony pelvis, indicating a degree of fusion greater than that usually present in such twins.
7. The pregnancy and labor of Rosa is a unique occurrence in the history of joined twins.

INFECTIOUS SARCOMA ("VENEREAL GRANULOMA") OF THE VAGINA IN DOGS *

EMIL NOVAK, M.D.

AND

ROBERT GLENN CRAIG, M.D.

BALTIMORE

We recently observed in a dog the occurrence of a vaginal growth which histologically resembled a sarcoma, but which clinically possessed certain characteristics which were rather hard to reconcile with such an interpretation. This condition presents such interesting characteristics between genuinely neoplastic and inflammatory pseudoneoplastic lesions that it seems strange that it has not been studied more intensively. Veterinarians have long been familiar with the lesion, and a number of interesting contributions are available in the literature, but the subject has not yet been cleared up.

CLINICAL CHARACTERISTICS

According to Beebe and Ewing,¹ the condition occurs most frequently in young and middle-aged dogs. Williams² states that until recent years it had not been extensively observed in America and that it appears to have been imported, notably through English bulldogs. However, this fact is probably not indicative of any especial susceptibility of this breed. As a matter of fact, many cases are reported in various other breeds. The disease affects both males and females. In the former, the lesion is usually noted first in the region of the corona. In the latter it appears first as a nodular growth, frequently multiple, on some portion of the vagina, often near the urethral orifice. With increasing size the growths tend to become pedunculated. At first there is little or no infiltration of the deeper tissues, but in the later stages this feature becomes marked. According to most observers, the condition is not characteristically preceded or accompanied by a vaginal discharge, although superficial ulceration with bleeding is common. Involvement of the inguinal glands and the occurrence of metastasis to distant points (abdominal wall, peritoneum, liver, etc.) may be noted.

There appears to be a striking variation in the severity of the clinical picture. In the mild types the lesion seems to be essentially local, with

* From the Gynecological Department of the Johns Hopkins University Medical Department.

1. Beebe, S. P., and Ewing, James: A Study of the So-Called Infectious Lymphosarcoma of Dogs, *J. M. Research* **15**:209-220, 1906.

2. Williams, W. L.: Personal communication to the author.

little tendency to spread beyond the vagina, and easily curable by simple measures. In other published cases, on the other hand, the picture is that of a definitely malignant process, which progresses rapidly, with extensive metastases, resulting in the death of the animal. This variation in the clinical picture is no doubt partially, but only partially, explainable by the duration of the lesion. It is chiefly responsible for the fact that those who have observed only a case or two look on the lesion as a mild local disease or as a grave malignant infection, as the case may be. All authors, even those who look on the disease as definitely malignant, are agreed that it is spread from one animal to another through coitus. In early stages the condition is often readily curable by simple excision, or by curetting and cauterization, but in the later, more malignant types, even radical efforts at removal are likely to be unsuccessful.

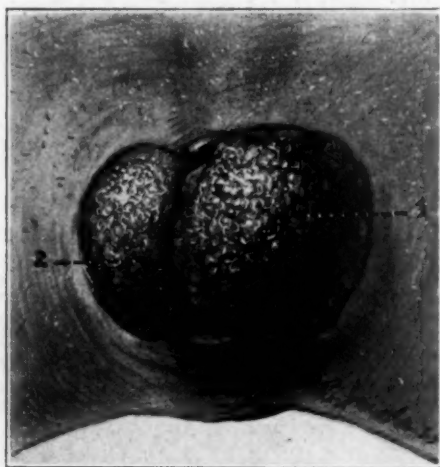


Fig. 1.—Vaginal walls retracted, better exposing surfaces of vaginal growths (Sept. 19, 1924).

Before reviewing the general subject, we shall present the case which furnished the incentive for this report.

REPORT OF CASE

History.—On Sept. 19, 1924, through the courtesy of Dr. John Wade, of this city, we examined one of the most prized animals of his kennels, a bitch of the pure English bulldog breed. She was 3 years old, and had apparently been in the best of health until three months previously. At that time she began to bleed vaginally, and this symptom had continued intermittently up to the time of examination. The bleeding more recently had been quite profuse at times, and several days before the examination a vaginal protrusion had made its appearance. The bitch had been bred but once, about one year previously, and then with a dog said apparently to have been free from venereal disease.

Examination.—The genitals were normal except for a polypoid mass about 1.5 cm. in diameter, which presented at the outlet. It was attached by a rather broad pedicle to the anterior vaginal wall, just below and a little to the right of the urethral meatus. On digital examination a second tumor of almost the same size and shape was found to spring from the anterior vaginal wall a little farther within the canal and to the left of the midline. Moreover, two smaller and more sessile outgrowths could be felt in the vaginal vault, close to the cervix.

When the animal was anesthetized these tumors were more clearly exposed, their general appearance and location being shown in figure 1. All the tumors were covered by what seemed to be a normal vaginal mucosa, although the lower two showed considerable reddening, with some ulceration near the lower pole. This was apparently due to the trauma incident to their partial delivery from the canal. The consistency of the growths was fairly firm.

Operation.—All four tumors were removed by simple excision. The oval wounds about the pedicle were closed with catgut sutures. The removal was local, no attempt at wide excision being made. There was no enlargement of any of the regional lymph glands and no further evidence of extension.



Fig. 2.—Low power magnification showing mantle of sarcoma cells surrounding central connective tissue core.

Subsequent Course.—Six months later an examination was made, although there had been no recurrence of the bleeding. The vagina was smooth except for a small, ovoid, sessile enlargement, about 1 cm. in diameter, in the vaginal vault. It was raised above the surface only about 0.5 cm. This was excised, as at the previous operation. No sutures were used, but the base of the growth was thoroughly cauterized with the actual cautery.

Microscopic Examination.—Numerous sections were made from the tumors, but the microscopic picture was essentially the same in all. In many of them the surface epithelium was intact, in others it was lost in some places. In these areas there was, of course, some superficial inflammatory reaction, although, taking the sections as a whole, evidences of the inflammation were conspicuous by their absence. In some areas the surface epithelium, though present, was quite thin. Immediately beneath the epithelium, crowding right up to the basement membrane, the characteristic tumor cells could be seen (fig. 3). They were round, quite uniform, with rather dark-staining nuclei. A pinkish granular cytoplasm was discerned in thin sections, or where the cells

were teased apart by edema. There appeared to be little intercellular substance, but in places the tumor cells had a slightly alveolar arrangement, with light trabeculae containing blood vessels. The tumor was moderately vascular, the blood vessels being chiefly rather small. The intima of these blood vessels was apparently intact, the other layers being replaced by tumor cells. A few small hemorrhages were also seen. Mitoses were numerous (fig. 4), some high power fields showing as many as six or eight. The limits of the tumor process were sharply circumscribed, although it was not encapsulated. This is shown in figure 2, where a sharp line of demarcation is seen between the tumor cells and the connective tissue core or stem, which is found beneath the mantle of sarcoma cells. Spirochetes have been reported in two instances, although

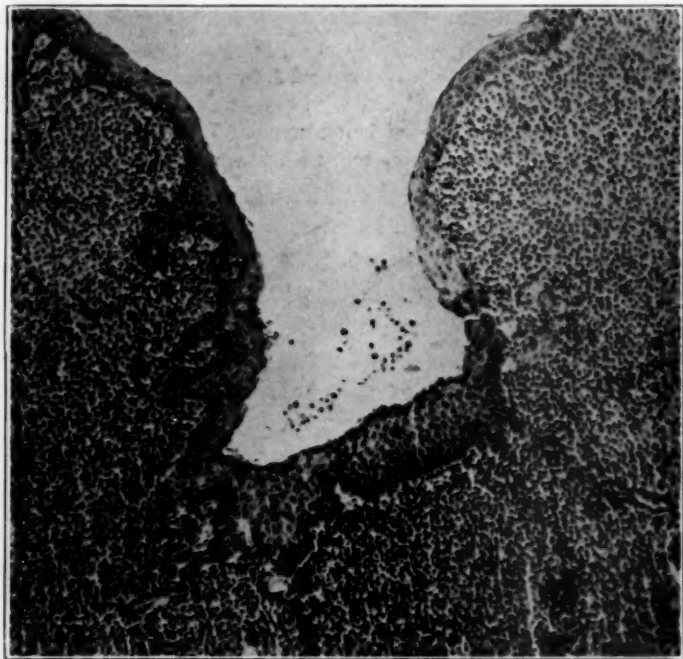


Fig. 3.—The intact stratified epithelium can be seen with the tumor cells immediately adjacent to the basement membrane; there are no inflammatory elements.

bacteria have been uniformly absent. Tissue stained with MacCallum's bacterial stain failed to show any organisms in our case. Levaditi's stain was negative for spirochetes.

Transplantation Experiment.—At the time of the removal of the recurrence of the original tumor, portions of it were transplanted in two dogs. In both animals the vagina was thoroughly scarified and bits of the tumor tissue rubbed in. A small portion of the growth was planted into the animals' abdominal wall, beneath the rectus fascia. The grafts were unsuccessful, so that the inoculation experiments which we had planned were not possible. We have been unable to secure any further tumor material, as the dog has apparently fully recovered.

A section of the tumor was examined by Dr. James Ewing, who reported that "the section shows the typical structure of the infectious sarcoma of dogs, which Dr. Beebe and I worked at many years ago. I think it is a true sarcoma and I think we proved this beyond question, in our article. The tumor is transplantable and grows from the transplanted cells. You ought to cure it with radiation."

We were especially anxious to secure the opinion of veterinary authorities on the lesion, because of the opportunities available to veterinarians for the study of the condition. Dr. W. L. Williams, of Cornell University, commented on the clinical characteristics of the

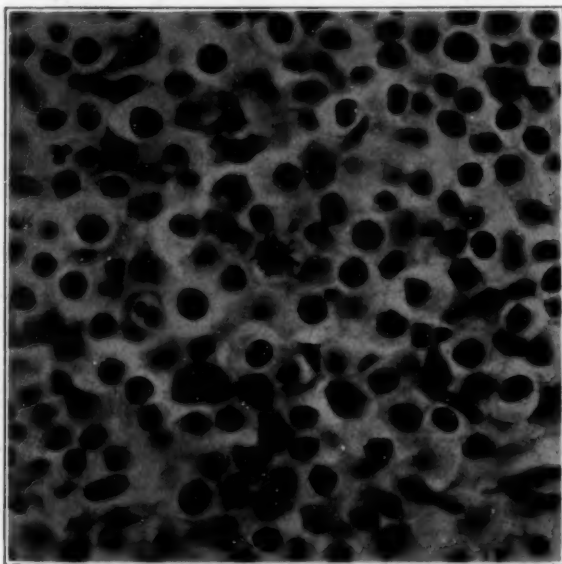


Fig. 4.—The tumor cells are round and uniform, with dark-staining nuclei; a mitotic figure can be seen in the center and two near the edge; mitotic figures are numerous; the cytoplasm is palely pink and granular; there is little intercellular substance.

tumor as follows "The clinical description of the vaginal tumor from a bitch corresponds in all essentials with the venereal granuloma of dogs. I carried the slide to Dr. S. A. Goldberg, the pathologist at the veterinary college, and he pronounces it typical in structure with these growths. A spirochaete has been observed associated with the tumor and one or two writers have suspected an etiological relation. So far as I know there is no substantial evidence that this is true—or untrue. There is very little literature upon the subject so far as known to me."

In a second communication he wrote that "The designation of granuloma probably arose from the clinical aspect of the growth, which

impressed some veterinarians as a mass of granulating tissue before any competent histological study had been made."

Dr. Frank H. Miller, official veterinarian of the American Kennel Club, wrote as follows: "The highly infectious nature of the dog granuloma to my mind places it in a class far removed from the sarcomata, irrespective of the microscopic findings, and I think this assumption is backed up by transplantation experiments. I have had considerable experience with this disease in dogs, and it all points to a specific cause which cannot be very closely allied to those giving rise to the sarcomata."

Finally, Dr. W. J. Lentz of the University of Pennsylvania, who also examined a slide, reported that "this is undoubtedly a small round cell sarcoma."

REVIEW OF THE LITERATURE

The literature of the subject is rather difficult of presentation in a clear-cut fashion, as there has been so much confusion in its nomenclature, particularly as to the two designations of infectious granuloma and sarcoma.

The first description of the condition appears to have been by Nowinsky,³ in 1876. This author reported the extirpation of a vaginal tumor in a bitch, followed by recurrence in three months. In one year it had become as large as a hen's egg, and showed ulcerative changes. In its neighborhood had appeared numerous other small, nonulcerated nodules. Microscopically the tumor showed a peripheral zone of dense connective tissue. From this there extended inward numerous septums, forming a fine fibrillary network, in the meshes of which were the tumor cells. These were chiefly round and about the size of white blood corpuscles. Others were oval, stellate or spindle-shaped. The blood vessels were rather poorly developed. The intercellular substance gave the reactions of mucin, and a diagnosis was made of myxosarcoma. The tumor was successfully transplanted into the thoracic subcutaneous tissue of an 8 day old puppy, the structure of the transplant being quite similar to that of the original growth. Successful inoculations were also made into a 14 day old puppy, and into one of 2 months.

Wehr³ (1888) was the second to describe successful transference, although he designated his tumor as a carcinoma. Duplay and Cazin³ (1894) appear to have been the first to suggest that the tumor might possibly be of inflammatory nature. In their case the animal's vagina contained three tumors about the size of a hazelnut. One of these, after removal, was rubbed into the scarified foreskin of two male dogs. In both animals tumors developed which were identical with the original growth. In one of the two, moreover, a tumor nodule appeared in the

3. Nowinsky, Wehr, Duplay and Cazin, and Geisler, quoted by Sticker.

testis. The general conclusion was to the effect that the growths were of inflammatory nature and somewhat analogous to condylomas.

Several spontaneous and several experimental tumors were reported by Smith and Washbourne⁴ (1898). Especially interesting are their observations on the remarkable venereal infectivity of the lesions. For example, a dog with a small growth on the penis, behind the cornua, served twelve bitches, of which eleven developed similar growths in the vagina. Again, a dog which had served two infected bitches conveyed the lesion to two healthy bitches, although he himself had not at that time shown any evidence of a growth on the penis.

The microscopic examination of the lesions studied in this series of cases showed a structure obviously identical with what was observed in our own case. It was interpreted by the authors as sarcoma. No secondary deposits were found in the viscera, although only two post-mortem examinations were performed. In one case only were the inguinal glands involved. Spontaneous cures were not noted. The rate of growth, according to Smith and Washbourne, is likely to be slow at first, but is more rapid later, when infiltration of the deeper parts may also occur. No evidence was found to suggest that the lesion is due to the prolonged irritation of a vaginal discharge, which was consistently absent in this series of animals. The treatment recommended is excision.

Geisler's³ (1895) report of several inoculation experiments is interesting chiefly because the author, like Wehr, concluded that the tumors are of carcinomatous nature.

Powell White's⁵ description (1902) of the histologic appearance of the tumors which he studied is almost identical with that given of our own specimen. He stated that they were made up of small round cells packed closely together, with a delicate lymphoid reticulum. The epithelium over the surface was intact, and the tumor was rather sharply circumscribed, though not encapsulated. He believed that these tumors differed from sarcomas in that they were very contagious, that they were much less malignant and that there was no infiltration of tissue, and rarely metastasis.

Passing over a number of less important reports, one comes to the valuable studies of Anton Sticker⁶ (1904 and 1906). His first case was observed in a 7 year old male fox terrier and was looked on as a round

4. Smith, G. B., and Washbourne, I. W.: Infectious Venereal Tumors in Dogs, *J. Path. & Bact.* **5**:99, 1898.

5. White, C. P.: Contagious Growths in Dogs, *Brit. M. J.* **2**:176, 1902.

6. Sticker, Anton: Transplantables Lymphosarkom des Hundes; ein Beitrag zur Lehre der Krebsübertragbarkeit, *Ztschr. f. Krebsforsch.* **1**:413, 1904; Infectiöse und krebsige Geschwulste an den äusseren Geschlechtsorganen des Hunds, *Arch. f. klin. Chir.* **78**:773-800, 1906.

cell sarcoma of the penis. Sticker was able to transplant this tumor into various regions, including the skin, peritoneum, scrotum, bone, spleen, etc. In the peritoneum the extension occurred along the surface, although the growth at times penetrated into the blood channels, with general sarcomatosis. Lymphogenous metastasis was far less common, but was noted in certain cases. The tumor cells were resistant. Their growth capacity was not destroyed either by storage on ice for twenty-four hours, even at -14°C ., or by warming to 50°C . for two hours. On the other hand, thorough mechanical crushing of the cells destroyed their activity. Efforts at transplanting the growth to other animals (cats, rabbits, guinea-pigs, rats and mice) were unsuccessful. Bacteriologic studies were all negative. Extensive inoculation experiments were carried out by Sticker, who concluded that the tumor was undoubtedly a round cell sarcoma.

Chronologically, the next important contribution is that of Bashford, Murray and Cramer⁷ (1905), who concluded that the lesion should be regarded as an infectious granuloma, because (1) it was infectious and contagious per coitum; (2) the cells originated from surrounding connective tissue, as could be shown by the presence of transition stages; (3) the process was similar to that seen after inoculation with the organisms of tuberculosis or glanders; (4) it occurred in young but sexually mature, rather than old, dogs.

The assertion that the cells of transplants grow from the surrounding tissues constituted the chief point of attack in the paper of Beebe and Ewing¹ (1906), who properly emphasized that this was the crucial test between a merely inflammatory lesion and a genuine neoplasm. Their studies led them to a conclusion diametrically opposite to that of Bashford, Murray and Cramer. They found that the cells in transplanted bits of the tumor did not entirely disappear, but that islands of intact cells always remained, showing mitotic activity from the very first day, and that these develop into definite tumor nodules. Their studies would appear to establish irrefutably the neoplastic nature of the lesion. While they did not believe that there was yet sufficient evidence to speak arbitrarily as to the correctness or incorrectness of the parasitic theory of origin, they pointed out that, as Sticker showed, "all those means of communication which destroy the integrity of the tumor cell stop at the same time its infectiousness."

No further contributions of importance have been made, although numerous short reports of cases are available in the literature. Most of these, however, devote little or no attention to the pathology of the condition.

7. Bashford, Murray and Cramer: Reports of Imperial Cancer Research Committee, 1905, no. 2.

It is obvious, from what has been said, that the clinical characteristics of many of the less severe types of this canine lesion are difficult to reconcile with our ordinary conception of sarcoma. And yet, from a histologic standpoint, no other interpretation seems possible. Little is to be gained by comparison of the canine tumor with sarcoma of the vagina or cervix in man. It is of interest, perhaps, to note that in women sarcoma of the vagina, and even more often, sarcoma of the cervix, is apt to assume a distinctly polypoid form. In a certain proportion of the human cases, illustrated beautifully in a case recently reported by Kuncz and Zacher,⁸ the microscopic picture is quite similar to that of the canine growth, although here the analogy ends, for the human growth invariably runs the usual course of malignancy. Furthermore, genuinely granulomatous growths, occasionally are observed in the human vagina, but there seems no justification for comparing them with the tumor under discussion, inasmuch as they present a totally different microscopic picture.

Certainly there is nothing in the sections which we have studied, nor in any of those described or pictured in the literature, which suggests an inflammatory process. It would be unusual for a purely inflammatory lesion to occur in the form of such definite nodules, springing from otherwise normal vaginal mucosa. There seems to be no histologic difference between the clinically mild cases, without metastasis, and those in which the disease infiltrates surrounding tissues, undergoes metastasis and causes death. Cases of the latter type suggest sarcoma, both clinically and structurally. Furthermore, the study of Beebe and Ewing, already quoted, has apparently established that the cells of transplanted portions of the tumor do not arise from the native cells of the tissue, but from the actual surviving cells of the tumor proper. Again, Sticker has shown that the destruction of the tumor cells renders inoculation unsuccessful. He urges that the apparent infectiousness of the tumor is paralleled by the occurrence of "cancer a deux," as well as by the seeming auto-inoculability of cancer of one lip to another, or of one labium to the other. All in all, the evidence seems to favor the view that these tumors are of sarcomatous nature, although, as stated at the onset, they present certain clinical characteristics which one would scarcely expect to find in malignant growths.

SUMMARY

A case is reported of the interesting borderline lesion which veterinarians commonly designate as "venereal granuloma," but which pathologically exhibits genuinely sarcomatous, rather than inflammatory

8. Kuncz, A., and Zacher, P.: Sarcoma Polyposum Uteri, Arch. f. Gynäk. 123:211-218, 1925.

characteristics. It affects the genitals of either male or female dogs, and is transmitted through coitus. There is much variation in the degree of malignancy, if we may judge from published reports. In some cases, it progresses rapidly, exhibits metastases and causes death. More frequently, as in our case, its course is relatively benign, the lesion being curable by excision, by excision plus cauterization or by radium (Ewing). The tumor has been successfully transplanted by various investigators. The chief point at issue has been whether or not these tumors are genuinely neoplastic, i. e., sarcomatous. The weight of evidence, particularly that yielded by the transplantation experiments of Beebe and Ewing, is definitely in favor of the view that this lesion, from a pathologic standpoint, is properly classified as a sarcoma.

POSTCAVAL URETER

A REPORT OF TWO CASES IN MAN *

VICTOR C. JACOBSON, M.D.

ALBANY, N. Y.

Among the causes of hydronephrosis are those which are congenital, such as kinks of the ureter from anomalous bands or malposition of the kidney. Other cases result from anomalous arteries which compress the ureter, and cause intermittent obstruction with resulting hydrops of the tract above. The object of this report is to record two examples of an abnormality of the ureter in man, which apparently has not been described in this country; i. e., a ureter which, in its course, passes between the inferior vena cava and the aorta—one case in a man, causing unilateral hydronephrosis, and the other in a year old infant who also had many other congenital defects.

REPORT OF CASES

CASE 1 (fig. 1).—G. H., a white man, aged 72, a mental patient in Pavilion F of Albany Hospital, entered Feb. 16, 1926 and died four days later, with symptoms and spinal fluid indications of acute suppurative meningitis. No urine could be obtained because of incontinence. Autopsy disclosed a temporal lobe abscess from extension of a middle ear infection, and marked generalized arteriosclerosis. The following condition was also found. The kidneys were in normal positions. The right weighed 220 Gm., the left 180 Gm. The pelvis and upper half of the right ureter were markedly dilated down to a point at which the ureter emerged from between the vena cava and the aorta, 4 cm. above the bifurcation of the aorta. The pelvis and ureter in this way formed a letter S. The ureter opened into the bladder in a normal manner. The right spermatic vein emptied into the right renal vein, the left spermatic vein into the left renal vein. The right spermatic artery branched off the aorta. An anomalous artery ran from the aorta to the lower pole of the left kidney and was crossed anteriorly by the left ureter. There was marked arteriosclerosis with calcification of the aorta, but less disease of the renal and spermatic arteries. A moderate degree of hydronephrosis of the right kidney and arteriosclerotic nephritis of both organs were disclosed. There was atrophy of the wall of the right ureter where it was pinched between vena cava and aorta.

CASE 2 (fig. 2).—A male infant, aged 1 year, presented symptoms of congenital heart disease, second degree hypospadias and a widely open anterior fontanel. Autopsy disclosed dextroposition of the aorta, pulmonic stenosis, open interauricular and interventricular septums, a slightly patent ductus arteriosus Botalli, absence of the left kidney and left renal artery, a rudimentary left ureter arising from right ureter and defective development of the third lumbar vertebra. In addition there was the following condition. The right kidney was slightly larger

* From the Pathological Laboratory of Albany Hospital and the Department of Pathology of Albany Medical College.

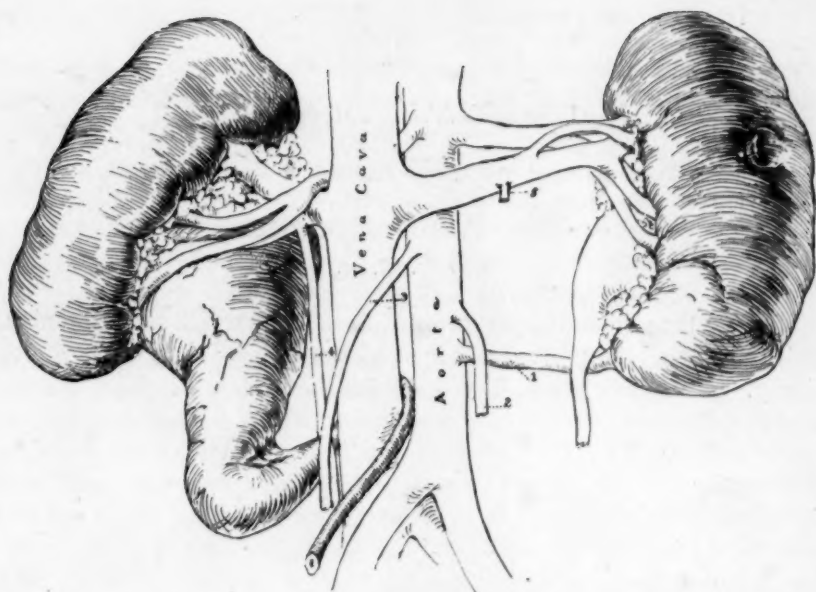


Fig. 1.—The postcaval ureter in case 1, with hydro-ureter and hydronephrosis; 1, indicates anomalous left renal artery; 2, inferior mesenteric artery; 3, right spermatic artery; 4, right spermatic vein; 5, left spermatic vein.

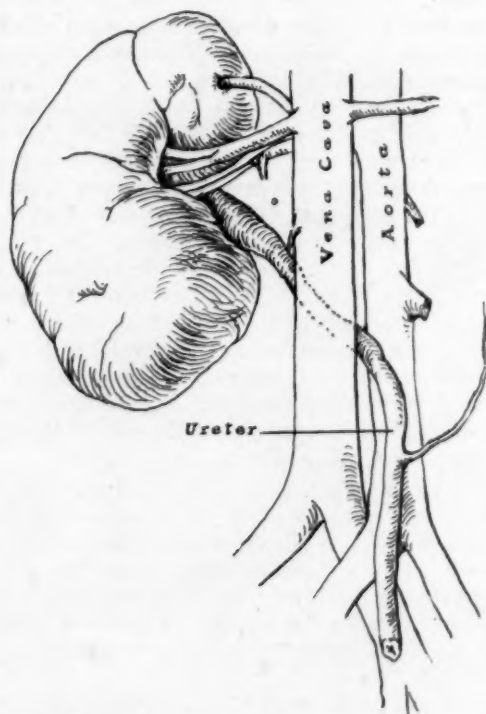


Fig. 2.—Postcaval ureter in case 2, showing the left ureteral cord joining the right ureter.

than normal. Its ureter passed between the inferior vena cava and aorta at the level of the inferior mesenteric artery, but with no evidence of obstruction. There was no recognizable left renal artery, unless a small stenotic vessel may be regarded as such. The left spermatic artery arose from the aorta, the right spermatic artery arose from the right renal artery, and the left spermatic vein emptied into the inferior vena cava. A left renal (?) vein at the level of the right renal vein passed into a mass of fat and connective tissue having no resemblance to a kidney.

In the first case the kidneys were in normal positions. The right ureter passed between the aorta and the inferior vena cava, about 4 cm. above the iliac bifurcation where it was compressed and the walls atrophied. The pulsations of the two great vessels may have contributed to the narrowing of the lumen. The left ureter was normal and lay anterior to an anomalous renal artery but the renal pelvis on that side was not dilated. There was marked sclerosis and calcification of the descending aorta, and the loss of elasticity so entailed may have been a factor in the late development of ureteral obstruction.

Hydronephrosis produced by an anomalous renal artery has been described by several observers, among them Kussmaul,¹ Mayo, Braasch and McCarty,² McDonald,³ Ekehorn⁴ and others. Ekehorn in reviewing twenty-five cases found the accessory vessels anterior to the ureter in 64 per cent and posterior in 28 per cent. A sagging of the kidney would place the ureter in more intimate contact with the artery and thus favor obstruction. Quain⁵ states that irregularity of renal arteries can be found in 25 per cent of bodies, an occurrence frequent enough to make it of clinical importance, as the foregoing papers testify.

The ureters in case 1 opened in the bladder in the normal manner. Apparently there had been no clinical symptoms referable to the unilateral hydronephrosis. Case 2, with its multiple cardiac and other defects, also presented striking errors in the development of the urinary tract, from unsymmetrical kidney at one end to hypospadias at the other. A fairly large but otherwise normal right kidney possessed a ureter passing downward between the inferior vena cava and aorta in the same manner essentially as in case 1, although no hydronephrosis had

1. Kussmaul, Adolf: Hydronephrosis durch Kreuzung des rechten Ureter mit einer überzahligen Nierenarterie, Würzburg, med. Ztschr. **4**:24, 1863.

2. Mayo, W. J.; Braasch, W. F., and McCarty, W. C.: The Relation of Anomalous Renal Blood Vessels to Hydronephrosis, J. A. M. A. **52**:1383 (May 1) 1909.

3. McDonald, A. L.: Anomalous Renal Arteries and their Relation to Hydronephrosis, Ann. Surg. **52**:814, 1910.

4. Ekehorn, G.: Die anomalen Nierengefäße können eine entscheidende Bedeutung für die Entstehung der Hydronephrose haben, Arch. f. klin. Chir. **82**: 955, 1907.

5. Quain: Anatomy, New York, Longmans, Green & Co., vol. 2.

occurred. The ureter was really double, the other limb being represented by a fibrous cord. The two united just above the iliac bifurcation and the common trunk opened into the bladder at the normal place for the right ureter. The left kidney failed to develop, presumably on account of the absence of its main nutrient artery.

The unusual course of the ureters described above is exceedingly rare. In 1911, Gladstone⁶ in reporting one case could find but three others in the literature, and none has been recorded since. Kolisko⁷ describes a case similar to case 1, in a man, aged 55, in which there were hydronephrosis and dilatation of the pelvis and ureter above the

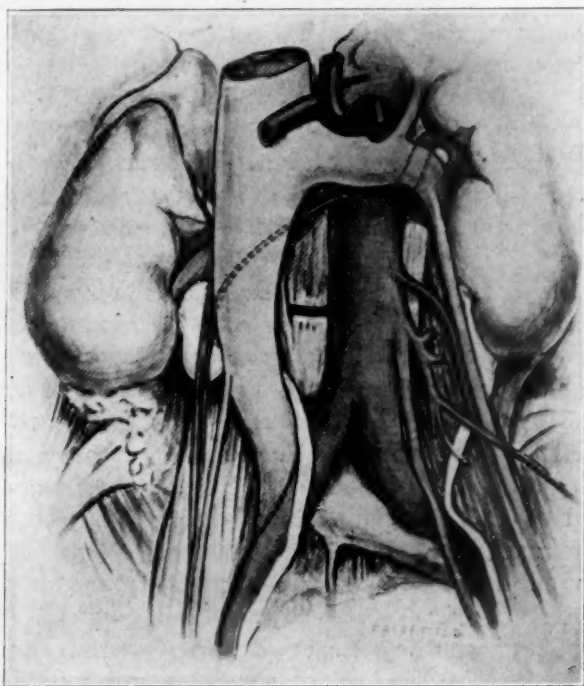


Fig. 3.—Drawing of specimen reported by R. J. Gladstone, showing the right ureter and right spermatic artery passing behind the inferior vena cava.

point at which the ureter passed behind the inferior vena cava. There was also a double renal vein on that side. Hochstetter⁸ reports a case in an infant a few weeks old, and also one in a cat. In the cat, the

6. Gladstone, R. J.: A Case in Which the Right Ureter Passed Behind the Inferior Vena Cava: with a Short Note upon a Case in Which the Left Renal Vein Passed Behind the Abdominal Aorta, and the Bearing of these Abnormalities on the Development of the Abdominal Veins, *J. Anat. & Physiol.* **6**:225, 1911.

7. Kolisko, F.: Ein Fall abnormen Verlaufe des rechten Ureters, *Anat. Anz.* **34**:520, 1909.

8. Hochstetter, Ferd, quoted by Gladstone (footnote 6).

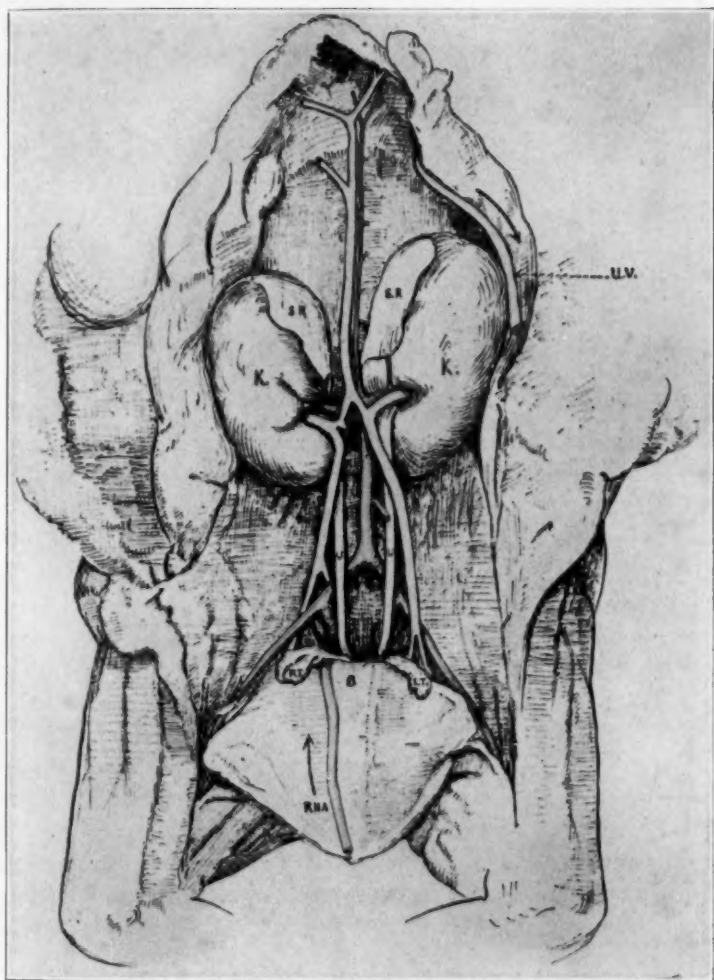


Fig. 4.—The abdominal blood vessels of an acardiac fetus, in which the ureter on each side passed behind the principal vein (Gladstone).

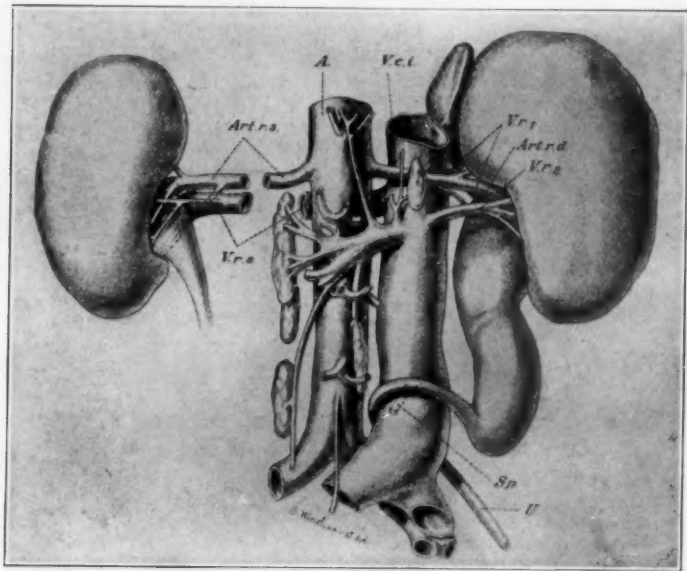


Fig. 5.—Posterior view of right postcaval ureter, Kolisko's human case, with hydronephrosis; *U* indicates the ureter; *Sp.*, the right spermatic vein.

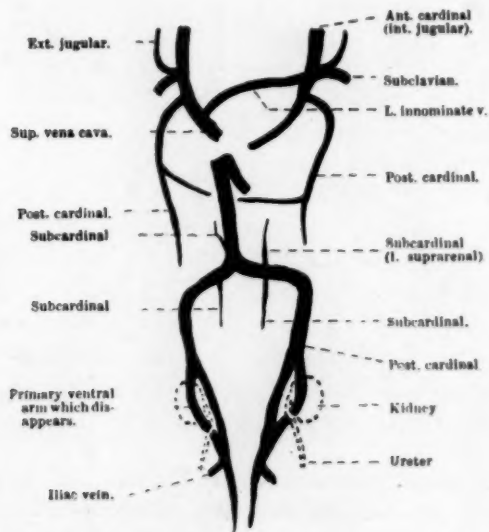


Fig. 6.—The relations of the kidney and ureter to the abdominal veins (Hochstetter); persistence of the ventral arm of the venous circle about the kidney, and disappearance of the dorsal arm, would result in postcaval ureter.

inferior vena cava was double as far as the entrance of the renal veins. The ureter on each side lay behind the corresponding vein, which he regarded as the persistent Wolffian section of the posterior cardinal vein.

McClure⁹ and Bunting¹⁰ have each seen a postcaval ureter in the cat, and Graves¹¹ in both the rabbit and the cat.¹² And here again is a striking illustration of the "law" of dual coincidence, familiar to pathologists, in which the uncommon things so often occur in pairs, for in a small autopsy service the condition was observed twice in a few months, the second case appearing while this report was being written.

What is the explanation of this position of the ureter from the standpoint of developmental embryology? The ureter begins as a tubular diverticulum from the Wolffian duct close to the point at which the latter joins the cloaca. It is seen first before the definitive veins appear and grows from behind forward, dorsal to the body cavity. As the ureter increases in length, it becomes separated from the Wolffian duct and acquires a distinct opening into the anterior part of the cloaca nearer the head of the embryo than that of the Wolffian duct. The part of the cloaca receiving the ureters becomes the bladder. The upper end of the ureter becomes the pelvis and calices of the kidney.

Hochstetter, in describing his case, explains the anomaly in this manner. At an early stage of development the kidney and its ureter grow up from the lower end of the Wolffian duct, behind and internal to the posterior cardinal vein. The cardinal vein is thus primarily ventral to the ureter. An anastomosing branch is later formed dorsal and mesial to the ureter. This anastomosing branch joins the main vein above and below the ureter, forming a venous ring around it. Afterward the primarily ventral portion of the venous ring disappears, and the dorsal portion, which has become enlarged, persists on the right side as the permanent inferior vena cava, and lies internal to the ureter. However, should the primary condition persist, the ureter will be behind the inferior vena cava, and pass downward internal to the vena cava and between it and the aorta.

Gladstone, however, is inclined to believe that the anomaly of postcaval ureter is due to the enlargement of an anastomosis between the posterior cardinal vein and the subcardinal vein, taking place below the point at which the kidney and ureter pass between the two vessels, instead of above this point.

9. McClure, C. F. W.: On the Frequency of Abnormalities in Connection with the Post-Caval Vein and its Tributaries in the Domestic Cat, *Am. Naturalist* **34**:185, 1900.

10. Bunting, C. H., personal communication to the author.

11. Graves, R. C., and Davidoff, L.: Anomalous Relationship of the Right Ureter to the Inferior Vena Cava, *J. Urol.* **8**:75, 1922.

12. Dr. Bunting has allowed me to use the diagram of the condition he found in the cat in 1894.

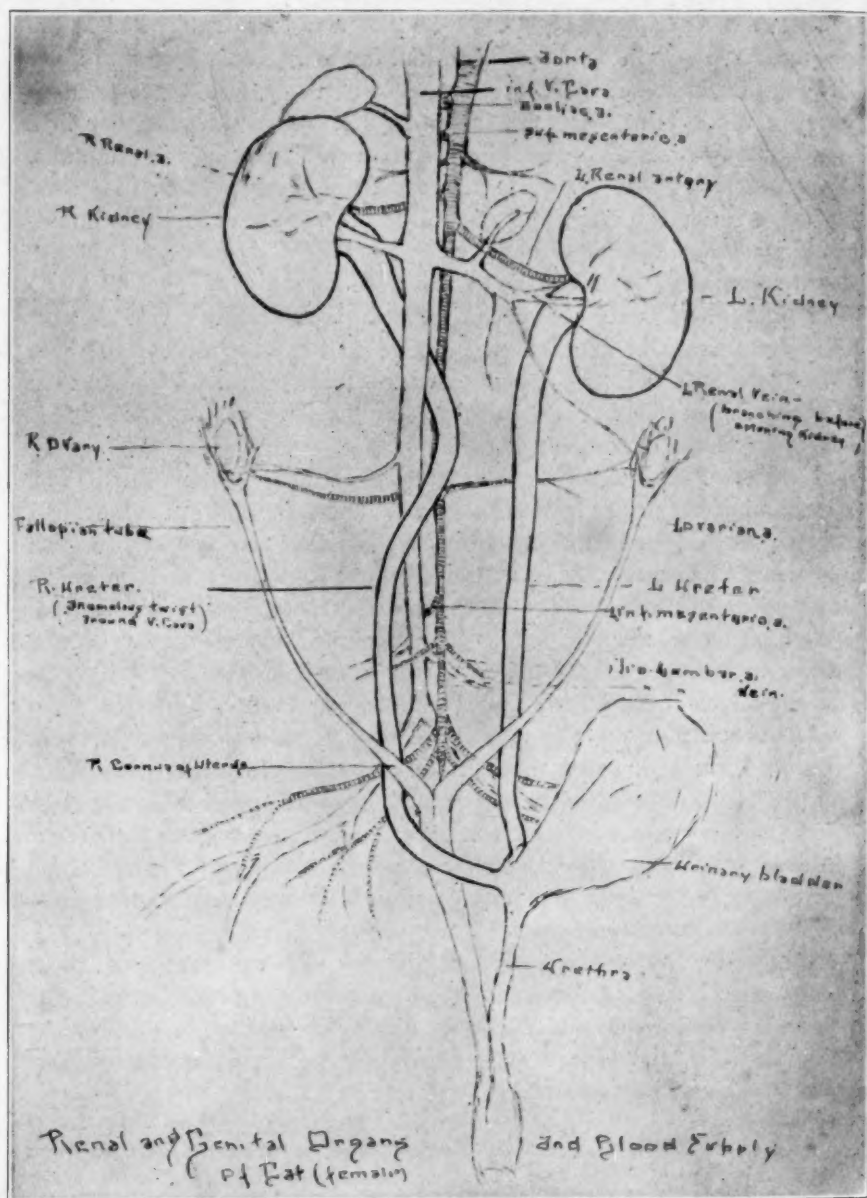


Fig. 7.—Drawing loaned by Dr. C. H. Bunting, from an observation of post-caval ureter in the the cat made in 1894.

Graves quotes McClure on postcaval ureter to the effect that "it represents an instance in which the embryonic posterior cardinal vein of the right side has persisted as the portion of the inferior vena cava which lies caudal to the level of the renal veins." Incidentally, all cases of postcaval ureter reported, including my own, have been on the right side.

SUMMARY

1. Two cases of postcaval ureter in man are described, one in an adult and the other in an infant, aged 1 year, with multiple congenital defects.
2. In the adult hydronephrosis was present, but of late onset, and probably developed *pari passu* with the sclerosis and calcification of the abdominal aorta. In the infant with normal aorta no narrowing had occurred.
3. Apparently, these are the first two cases in man in the American literature, bringing the total of reported human cases to six.
4. Several theories are presented to explain postcaval ureter from the standpoint of developmental embryology.

GLUCOSE TOLERANCE IN PATIENTS WITH VAGOTONIA *

JOHANNES M. NIELSEN, M.D.

AND

WELCOME B. LEWIS, M.D.

BATTLE CREEK, MICH.

That patients with vagotonia manifest a high tolerance for carbohydrates was established ¹ more than a decade ago and is well known; but the mechanism of this peculiar property has been obscure and has now aroused the interest of workers in this field.

It has been shown ² that patients suffering from vagotonia (whether it is secondary to a psychosis, neurosis, infection or long-continued overwork) experience, with peculiar regularity, a hypoglycemic reaction during the course of a glucose tolerance test. The symptoms of these reactions in order of frequency are: excessive hunger, dizziness, weakness, sweating, seeing spots, tremor, collapse with blood pressure too low to record, amblyopia and stupor. The close similarity of these reactions to the effects of an overdose of insulin impressed us; we felt certain that these attacks and insulin reactions were of identical origin.

Our conception of the production of vagotonia is as follows: When it is secondary to psychosis or neurosis, the disorder is based on emotional disturbances. When it is secondary to exhaustion, we believe that the long-continued use of the sympathetic side of the vegetative system and the endocrine glands for purposes of dealing with the outside world, together with loss of sleep, rest and rehabilitating influences presided over by the greater vagus nerve, has caused the sympathetic system to become weakened, and to produce an imbalance manifested by the overactivity of the vagus nerve. It is thus not actually an *overactivity* but an *uncontrolled activity* that causes the symptoms. As W. H. Riley has said, vagotonia might better be called sympathicotonia (atony of the sympathetic system). The effect of the imbalance, however, is identical with stimulation of the vagus in the presence of a normal sympathetic system.

Britton ³ has shown that stimulation of the right vagus nerve in cats produces hypoglycemia as long as the stimulation is maintained. He has

* From the Clinic of the Battle Creek Sanitarium.

1. Eppinger and Hess: *Vagotonia*, transl. by Krause and Jelliffe, *Nervous and Mental Disease*, Monograph Series 20.

2. Nielsen, J. M.: *Vagotonia and Hypoglycemic Reactions*, *J. Nerv. & Ment. Dis.* **63**:456, 1926.

3. Britton, S. W.: *Studies on Conditions of Activity in Endocrine Glands; Nervous Control of Insulin Secretion*, *Am. J. Physiol.* **74**:291, 1925.

demonstrated that the action is specifically caused by the effect of this stimulation on the pancreas. Since it is impossible to perform an experiment of this kind on a person some less direct method must be used for determining whether or not there is an overproduction of insulin in patients with vagotonia.

Foshay ⁴ has shown that following the parenteral injection of insulin into the system, the characteristic blood changes consist in a lowering of blood cell sugar from three to six times as great as the lowering of the plasma sugar. Such an injection is obviously not identical with a slow, steady secretion from the pancreas; yet if these effects could be demonstrated in patients, they would point to the action of insulin.

In carrying out the work, there was a preliminary question to be settled. Since we were to deal with differences in plasma and cell sugar,

TABLE 1.—Results of Injection of Insulin with Fluoride as Anticoagulant

	Time Before Centrifugalizing in Minutes							
	1	12½	34	50	61	66	72	79
Whole blood (mg. %)	48	46	50	56	66	56	56	49
Plasma	44	41	44	39	50	48	44	50
Cells	52	52	56	72	80	65	67	67
Cell minus plasma	8	11	12	35	30	17	23	17

TABLE 2.—Results of Injection of Insulin with Oxalate as Anticoagulant

	Time Before Centrifugalizing in Minutes						
	¼	29	34	48	60	65	80
Whole blood (mg. %)	46	40	56	56	55	56	49
Plasma	42	36	49	45	44	44	49
Cells	50	45	66	60	67	60	49
Cell minus plasma	8	9	17	24	23	25	0

and with differences produced by the action of insulin, it was important to ascertain that no diffusion occurred in vitro before the centrifugalization could be done. To determine this point, a person was given an intravenous injection of five units of insulin immediately after control specimens of blood had been withdrawn. As soon as we had reason to expect a marked difference in plasma and cell sugar (manifested clinically by weakness in the knees and tremor), samples of blood were withdrawn. These were kept for various periods of time before centrifugalizing. Two types of anticoagulants were used, (1) sodium oxalate and (2) sodium fluoride and thymol in order to have a check and to determine which was more satisfactory for the purpose in hand. The results are shown in tables 1 and 2.

4. Foshay, Lee: Observations upon the Action of Insulin on the Blood with Special Reference to the Cause of the Condition Known as Hypoglycemia, *Am. J. Physiol.* **73**:470 (July) 1925.

It will be seen that no diffusion occurred in the "fluorided" blood even after seventy-nine minutes, the longest time allowed. If there were any change, the tendency for about an hour in both "fluorided" and oxalated blood was in the other direction—an increase of cell sugar. The difference between cell and plasma sugar was 8 in one minute and 17 at the end. In the oxalated blood the differences were well maintained in the sixty-five minute specimen, but complete diffusion had occurred at eighty minutes when all specimens were alike. Therefore, in our subsequent work with fluorided blood we did not hesitate to allow thirty minutes to elapse before centrifugalizing, if this proved convenient.

A series of twenty-three patients with vagotonia was studied, and special attention was given to their glucose tolerance. All tests were conducted by giving the patient 100 Gm. of glucose in solution after a control specimen of blood had been taken. Other specimens were then taken at half, one, two, three and four hours after ingestion of the glucose. Separate whole blood and plasma sugar determinations were made and from these data, together with the cell percentage by volume, the cell sugar was calculated. The technic was as follows:

TABLE 3.—Results of Experiments on Glucose Tolerance in Twenty-Three Patients

		No. of Cases
Cell sugar drop 2 or more times that of plasma sugar drop.....	{Reaction.....	1
	{No reaction.....	2
	{Reaction ?.....	2
Plasma drop 2 or more times that of cell sugar drop.....	{Reaction.....	4
	{No reaction.....	2
Neither of above.....	{Reaction.....	9
	{No reaction.....	3
		23 23

In 2 cc. of whole blood the sugar was determined by the method of Folin and Wu.⁵ A small amount was used for the determination of the percentage by volume of cells and plasma by the hematocrit. The remainder of the blood was centrifugalized, and the clear plasma obtained, in 2 cc. of which the sugar was determined as on the whole blood.

In order to determine whether Foshay's partition had occurred in our curves, the percentage per hour drop was to be calculated. But since this rate changes constantly during a glucose tolerance test, we agreed on the hour to be used in making our calculations. Since we should expect the greatest hypoglycemia to occur at the time of the reaction seen clinically we selected this time for the determination. In the cases in which no reaction occurred, or when this point was unknown, the point of lowest whole blood sugar level was chosen. The observations in the twenty-three cases are presented briefly in table 3.

A peculiar result was observed. The typical insulin reaction of Foshay occurred in only five of the twenty-three cases. (We have

5. Folin and Wu: A System of Blood Analysis, J. Biol. Chem. **38**:81 (May) 1919.

allowed a factor of 2 instead of Foshay's 3 which otherwise would have lowered our percentage still further.) The reverse occurred in six. In twelve others—a number greater than the other two combined—the typical insulin reaction of Foshay does not occur. We must therefore admit that Foshay's partition does not occur with any degree of regularity in cases of vagotonia either with or without a hypoglycemic reaction experienced in the course of a glucose tolerance test. We have no proof here according to Foshay's theory that the reactions are caused by an overproduction of insulin.

Have we proof that insulin is *not* the cause of the hypoglycemia and reactions? We believe not. On the contrary, we feel that the reactions are caused by insulin; but further knowledge of its action is necessary before definite proof can be obtained. The evidence on which our belief is based is here presented. (In this discussion our series is reduced to twenty-one by two cases in which we do not know whether or not a reaction occurred.) First, in every case in this series the cell sugar was falling at the time of a reaction or lowest point in the curve. Second, of the twenty-one patients, fifteen (77.4 per cent) experienced hypoglycemic reactions during the tests. All but two had the reaction at the time when the blood sugar was at its lowest. Much could be said of these two, both of which were peculiar, but for the present we shall consider them as exceptions. A large majority experienced reactions at the point of greatest hypoglycemia. Third, in the cases in which there was a reaction, the blood sugar at the time of the reaction averaged 63 mg. per hundred cubic centimeters. In those without a reaction, the average low point was 74 mg. per hundred cubic centimeters. Reactions are more common when blood sugar is lower. Fourth, the clinical symptoms during a reaction are identical with symptoms occurring after overdosage with insulin, and the patients recover quickly from the reaction if given sugar.

TYPE OF CURVE IN VAGOTONIA

In an effort to find some constant characteristic of the vagotonic curve the question has been studied from the following angles: absolute height of curve, rate of ascent, rate of descent, percentage drop per hour of cell sugar and plasma sugar separately, total fluctuation in curves, and absolute low points. The last named was the only feature which was fairly constant. The low point for all cases ranged from 41 to 83 mg. per hundred cubic centimeters, the average being 66.7 mg. per hundred cubic centimeters. All the other factors varied within wide limits. By averaging all the third hour values, the figure 74.5 mg. per hundred cubic centimeters was obtained, the range being from 50 to 95 mg. per hundred cubic centimeters. The values at the final hour averaged 79, with a range from 61 to 100 mg. per hundred cubic centimeters. A value as low as 41 was obtained at the second hour. There were

thus a few that dropped exceedingly low, and a few that did not fall below 80 at the third hour; but of the seven in which the whole blood sugar value was above 80 at the third hour, five were lower at some other time. These patients experienced their reactions at the lowest point. In addition to these observations, thirty-seven common symptoms were studied with a view to finding some consistency between certain symptoms and types of curves. None was found.

One unusual case is worthy of notice. The patient collapsed completely at the second hour, while the whole blood sugar was 105 mg. per hundred cubic centimeters. This is the anomaly which so many clinicians have noted in persons with diabetes—a hypoglycemic reaction without hypoglycemia. This was the point that Foshay attempted to explain on the basis of a cell sugar decrease far in excess of the plasma sugar decrease. In the present instance the cell sugar dropped from 184 mg. to 88 mg., or a 52 per cent drop, while the plasma sugar was dropping from 175 to 115 mg., or a 34 per cent drop. This, however, does not conform with Foshay's statement that the cell sugar should fall from three to six

TABLE 4.—Reaction After Ingestion of Glucose

Degree of Reaction	Number of Cases	Average Low Point	Grand Average
0	6	76	76
+	4	62	63
++	6	61	
+++	3	69	
++++	2	63	
Unknown	2	72	72

times as rapidly as the plasma sugar. The patient was white, pulseless, perspiring profusely and too weak to raise a limb, while the whole blood sugar was 105 mg. per hundred cubic centimeters. He improved constantly without aid by the next hour, when the blood sugar was 95 mg. per hundred cubic centimeters, and had recovered completely after another hour, when the blood sugar was 73 mg. per hundred cubic centimeters. Cannon and his co-workers⁶ have shown that a reaction consists in an overactivity of the sympathetic system when the blood sugar falls too low. We believe that a mechanism, probably complicated, comes into play to bring about the reaction. It is these other physiologic factors which vary in different persons, and which make possible reactions in the presence of a normal blood sugar.

In this series there were three cases in which the blood sugar fell immediately after ingestion of 100 Gm. of glucose. This seems difficult to explain except by an excessively active pancreas which is stimulated easily and acts quickly. In one of these cases the highest point in the

6. Cannon, McIver, and Bliss: Studies on the Condition of Activity in Endocrine Glands, *Am. J. Physiol.* 69:46 (Jan.) 1924.

course of the test was found in the starvation specimen. In the others, the blood sugar later rose slightly.

The degree of reaction seems to bear no direct relation to the depth of the curve, severe reactions occurring at a fairly high point and slight reactions occurring at points quite low. This is shown in table 4.

CONCLUSIONS

1. The typical insulin reaction in the blood, according to Foshay (lowering of the cell sugar content three or more times that of the plasma sugar content) does not occur with any degree of regularity in persons with vagotonia who suffer from "hypoglycemic reactions."

2. The only definite statement that can be made concerning the type of glucose tolerance curve in persons with vagotonia is that a low point is reached somewhere. The average in this series was 66.7 mg. per hundred cubic centimeters, with a range from 41 to 83 mg. per hundred cubic centimeters.

3. The "hypoglycemic reaction" is not necessarily coincident with hypoglycemia. There is still some unexplained factor in the production of these reactions.

4. Degree of reaction bears no direct relation to depth of glucose tolerance curve.

THE ALCOHOLIC CONTENT OF THE HUMAN BRAIN

ITS RELATION TO INTOXICATION *

ALEXANDER O. GETTLER, PH.D.

AND

ARTHUR TIBER, B.S.

NEW YORK

In a nation trying to enforce alcoholic prohibition, it would seem unwarranted to do any research work on the alcoholic content of human organs and its relation to intoxication. Although alcoholic beverages are prohibited in this country, they are nevertheless used, and in many localities with little or no restraint. Use of the hip-pocket flask has increased manifold since the prohibition law was instituted. The number of "bootleggers" and "speak-easies" is multiplying daily, because of the enormous profits of the wares. It is, therefore, not surprising that intoxicated persons are encountered every day.

Intoxication may be the contributory cause to many fatalities, such as automobile and vocational accidents. One of the important questions, therefore, which the medical examiner's office must answer before the courts or the compensation referee, is whether the person was intoxicated at the time of the accident. In the past, no conclusive answer could be given to this question for two reasons: first, there were no accurate methods for the determination of alcohol in human organs and, second, no data were available by which intoxication could be established by the amount of alcohol present in the organs. We, therefore, set out to solve this problem. In a foregoing article, a quantitative method for the estimation of ethyl alcohol in tissues was outlined. In the present paper, we report the protocol on which we base our determination of intoxication by the alcoholic content of the brain.

SEQUENCE FOLLOWED IN CONDUCTING THE INVESTIGATION

A. What Organ or Organs Shall Be Used for Analysis?—It is evident at the outset that the stomach and intestinal contents are of no value, for the reason that alcohol has no effect on the internal organs until absorbed. The alcohol in the gastro-intestinal tract is still outside the body proper. It indicates merely that alcohol has been partaken of, but can in no way be taken as an index of intoxication. The liver, brain,

* From the Chemical Laboratories of the Pathological Department of Bellevue and Allied Hospitals and of the Chief Medical Examiner's Office of the city of New York.

lungs, kidneys, spleen and blood were analyzed for alcohol in several hundred cases. The histories of these cases revealed that the alcoholic content of the brain gives the best and most consistent indication of the degree to which the alcohol had influenced the subject in question. This is to be expected, as the condition of intoxication is caused by the alcohol acting on the brain centers.

B. What Is the Normal Alcohol Content of Brain Tissue?—The alcohol content of the organs of persons who have not partaken of any alcoholic beverage is still an open question. The following values have been given by various writers: Ford,¹ 0.0057 per cent in the blood of animals; Nicloux,² 0.001 per cent in guinea-pigs; Landsberg,³ from 0.028 to 0.083 per cent in rabbit muscle; Maignon,⁴ from 0.016 to 0.027 per cent in dog blood; Pringsheim,⁵ 0.044 per cent in rats, 0.018 per cent in rabbit blood; Schweisheimer,⁶ 0.0368 per cent in human blood. No faith can be placed in any of these figures because the methods used by the workers were not specific for ethyl alcohol. Either of two methods was used by them. The alcohol was isolated by distillation and then determined either as iodoform, or by titration with a standard solution of chromic-sulphuric acid. It is evident that there are many volatile compounds beside ethyl alcohol that give the iodoform reaction. It is also true that the distillates from tissues contain many volatile reducing substances which will react with the chromic acid standard. The values obtained by these methods, therefore, do not give the true alcoholic content. They do not even prove the presence of alcohol.

Some of the earlier workers, in trying to prove the presence or absence of ethyl alcohol in animal tissue, made use of such tests as Moore's, Schiff's, Nessler's, Lieben's iodoform, and the reduction of a mixture of sulphuric chromic acid. They arrive at opposite conclusions. A. and J. Bechamp,⁷ Rajewsky,⁸ Vitali,⁹ Albertoni,¹⁰ M. Nicloux,¹¹ Landsberg¹² and Stochlasa¹³ claimed that a small amount of alcohol is

1. Ford: *J. Physiol.* **34**:430, 1906.
2. Nicloux: *Thèse de Paris*, 1900.
3. Landsberg: *Ztschr. f. physiol. Chem.* **41**:505, 1904.
4. Maignon: *Compt. rend. Acad. d. sc.* **140**:1063, 1905.
5. Pringsheim: *Biochem. Ztschr.* **12**:143, 1908.
6. Schweisheimer: *Deutsches Arch. f. klin. Med.* **109**:271, 1912.
7. Bechamp, A., and J.: *Compt. rend. Acad. d. sc.* **75**:1830, 1872; **76**:836, 1873; **89**:573, 1879.
8. Rajewsky: *Arch. f. d. ges. Physiol.* **11**:122, 1875.
9. Vitali: *Ann. di chim. e di farm.*, series 4, **5**:113, 1887.
10. Albertoni: *Ann. di chim. e di farm.*, series 4, **6**:250, 1887.
11. Nicloux, M.: *Compt. rend. Acad. d. sc.*, series 10, **3**:841, 1896.
12. Landsberg: *Ztschr. f. physiol. Chem.* **41**:505, 1904.
13. Stochlasa: *Deutsche med. Wchnschr.* **6**:198, 1904.

present in animal tissue; while Arnheim and Rosenbaum,¹⁴ and Umber¹⁵ came to the opposite conclusion. The reason for this disagreement is again that the tests used are not specific for ethyl alcohol.

Using the method we suggested in the foregoing paper, we tried to throw more light on this question. Five hundred gram portions of brain tissue were distilled with steam in the usual manner and 800 cc. of distillate was collected. An aliquot portion of this distillate was titrated for its acidity. Another aliquot portion was oxidized with a mixture of sulphuric chromic acid and distilled, until 250 cc. of distillate was collected. This second distillate was similarly titrated for its acidity. Any increased acidity of the second distillate over the first may be due to the oxidation of ethyl alcohol to acetic acid. We cannot state with certainty that this acidity is due to acetic acid production. It may be due to the production of acid from some other volatile, but normal, brain substances. What we can definitely state, however, is that the alcohol present in normal brain tissue is as our figures show, or less, but never more.

Table 1 gives ten of our series of normal cases.

TABLE 1.—Results in Ten Normal Cases*

Case Number	Cc. Twentieth Normal Acidity before Oxidation for Entire Distillate	Cc. Twentieth Normal Acidity after Oxidation for Entire Distillate	Cc. Twentieth Normal Acidity Produced by Oxidation	Mg. of Alcohol Calculated from Acidity	Mg. of Alcohol in 1 Kg. Normal Brain Tissue	Percentage of Alcohol in Normal Brain Tissue
1	14.43	16.08	1.65	3.79	7.58	0.00076
2	12.32	13.75	1.43	3.29	6.58	0.00066
3	14.10	19.00	4.90	11.27	22.54	0.00225
4	23.23	24.85	1.62	3.72	7.44	0.00074
5	17.95	21.98	3.98	9.15	18.30	0.00183
6	12.32	16.67	4.35	10.00	20.00	0.00200
7	21.47	24.86	3.39	7.70	15.58	0.00156
8	15.84	20.45	4.61	10.60	21.20	0.00212
9	10.91	16.06	5.15	11.84	23.68	0.00237
10	16.74	19.80	3.06	7.04	14.08	0.00141
Average.....					15.70	0.00157

* The brain materials used in this investigation were not more than forty-eight hours old; no noticeable putrefaction had set in.

The figures in table 1 indicate that the average normal content of alcohol in brain tissue may be about 15.7 mg. per kilogram (0.00157 per cent). The highest value obtained is 23.68 mg. per kilogram (0.00236 per cent). As stated above, this does not prove positively that all or any part of this figure is alcohol. To date we have no absolutely specific test for alcohol when present in such traces. This work, however, definitely proves that if alcohol is present in normal brain tissue, it is always present in amounts of 25 mg. per kilogram or less. If we

14. Arnheim and Rosenbaum: Ztschr. f. physiol. Chem. 40:220, 1904.

15. Umber: Ztschr. f. klin. Med. 39:12, 1900.

compare our figures for the average amount of alcohol present in the brain (0.00157 per cent) with the values of previous workers, which range variously all the way up to 0.0368 per cent, we notice that our figures are much lower. The reason for this is that writers on this subject, using the dichromate titration method almost exclusively, have calculated all the reducing power of brain distillates to ethyl alcohol. In our method, only that reducing action which has yielded acidity was calculated as alcohol. This makes our method somewhat more specific than the older chromic acid titration method.

C. What Is the Alcoholic Content of the Brain of Partakers?—The method used for the estimation of ethyl alcohol in the brain tissue was that of Gettler and Tiber, described in a previous paper. The results are shown in table 2.

RESULTS OF INVESTIGATION

More than 6,000 human brains have been analyzed by us for alcohol during the last five years. In table 2 we have given the analyses of only thirty-two, in order to save space. There would be no advantage in showing all of them in tabular form, because they show exactly the same features.

The following facts were brought out by the quantitative analysis for alcohol in this series of more than 6,000 cases:

1. The brains of persons who have had no alcoholic beverages for at least ten days prior to death, by our method, show an alcohol content of from 0.0005 to 0.0025 per cent. This amount of alcohol is what one might signify as the normal alcohol content. It must be remembered, however, that these figures simply mean that there is volatile material in brain tissue which, on oxidation, will yield said acidity. Our only positive claim in this respect is that normal brain tissue never contains more than 0.0025 per cent of alcohol.

2. The alcohol content of the brains of persons who have consumed alcoholic beverages ranges from 0.005 to 0.6 per cent.

3. In all those cases in which there was an alcoholic content of the brain below 0.1 per cent the patients had been normal in all their actions, as determined by a history in each case before death. Abnormal physiologic conditions were never reported in these cases. We have designated such cases as "trace" or "one plus" (+).

4. In all cases, as far as we could determine by the history, in which there was an alcoholic content of from 0.1 to 0.25 per cent the patients had shown some physiologic disturbance, such as increased aggressiveness, more or less loss of sense of care, etc. As long as the alcoholic content was below 0.25 per cent, we have not yet encountered a patient who was described to us as being affected enough to be noticed by others

TABLE 2.—Results of Estimation of Ethyl Alcohol in Brain Tissue

Case	History	Cause of Death	Gm. of Ethyl Alcohol per Kilogram of Brain	Percentage of Alcohol in Brain	Arbitrary Classification
1	In hospital 12 days; no alcohol given	Heart	0.0062	0.0006	Absent
2	In hospital 18 days; no alcohol given	Mercury poisoning	0.0195	0.0019	Absent
3	In hospital 8 days; no alcohol given	Nephritis	0.0156	0.0015	Absent
4	In hospital 24 days; no alcohol given	Heart	0.0005	0.0009	Absent
5	In hospital 15 days; no alcohol given	Pernicious anemia	0.0116	0.0011	Absent
6*	Intoxicated; in hospital 3½ hours	Alcoholism	3.150	0.315	+++
7	Intoxicated; in hospital 2 hours	Alcoholism	5.780	0.578	++++
8*	Found dead; seen intoxicated ½ hour before	Alcoholism	2.980	0.298	+++
9	In hospital 8 hours; not intoxicated, but aggressive	Alcoholism	1.760	0.176	++
10	In hospital 3 hours; intoxicated	Alcoholism	2.890	0.289	+++
11	In hospital 4 hours; not intoxicated, but aggressive	Shot	2.040	0.204	++
12	Intoxicated; in hospital 2 hours	Fractured skull	3.540	0.354	+++
13	Intoxicated when fracture received; lived 14 hours	Fractured skull	0.550	0.055	+
14	Same as in case 13; lived 18 hours	Fractured skull	0.730	0.073	+
15	In hospital 5 hours; intoxicated	Alcoholism	3.010	0.301	+++
16	Not intoxicated; in hospital 8 hours	Fractured skull	0.110	0.011	Trace
17	Intoxicated; in hospital 5 hours	Fractured skull	3.660	0.366	+++
18*	Intoxicated; in hospital 1 hour	Fractured skull	2.930	0.293	+++
19	In hospital 1½ hours; not intoxicated, but carefree	Fractured skull	2.250	0.225	++
20*	In hospital 3 hours; intoxicated	Alcoholism	5.450	0.545	++++
21	Intoxicated 30 min. before death	Alcoholism	3.800	0.38	+++
22*	Intoxicated 45 min. before death	Hit by train	4.300	0.42	++++
23	Brought to hospital in coma	Alcoholism	2.690	0.269	+++
24*	Was drinking excessively to the end	Alcoholism	5.050	0.505	++++
25*	Intoxicated 25 min. before death	Hit by auto	3.420	0.342	+++
26*	Found dead; intoxicated 2 hours before	Alcoholism	5.250	0.525	++++
27	Not intoxicated	Heart	0.560	0.056	+
28	Not intoxicated	Gunshot	0.090	0.009	Trace
29	Not intoxicated; one drink 4 hours previous	Heart	0.410	0.041	+
30	Intoxicated 2 hours before death	Alcoholism	3.850	0.385	+++
31*	Not intoxicated; in hospital 6½ hours	Alcoholism	0.750	0.075	+
32	Not intoxicated but carefree	Stabbed	1.500	0.150	++

* Indicates habitues, others only occasional drinkers.

and described as intoxicated. We designated this class of cases as "two plus" (+ +).

5. When the alcohol content of the brain reaches above 0.25 per cent, running as high as 0.6 per cent, the person's equilibrium becomes unbalanced. In all of the cases in which we found over 0.25 per cent of alcohol the patients were reported to us as intoxicated. This set of cases we have designated as "three plus" (+ + +), from 0.25 to 0.4 per cent and "four plus" (+ + + +), from 0.4 to 0.6 per cent.

6. The degree to which a person is influenced depends on the quantity of alcohol in the brain at the time. Our series of cases seems to show that it is immaterial whether the person is an alcohol habitue or not.

From the experimental work as shown in table 2, we have classified all alcohol cases into five groups, according to the amount of alcohol found in the brain. This classification is shown in table 3.

TABLE 3.—*Classification of Alcohol Cases*

Classification	Gm. of Alcohol per Klogram of Brain	Percentage of Alcohol in in Brain	Physiologic Effect
Trace	0.050 - 0.200	0.005 - 0.02	Normal
+	0.200 - 1.000	0.02 - 0.10	Normal
++	1.000 - 2.500	0.10 - 0.25	Loss of sense of care; aggressive
+++	2.500 - 4.000	0.25 - 0.40	Loss of equilibrium; intoxicated
++++	4.000 - 6.000	0.40 - 0.60	Unbalanced; intoxicated

D. Is the Alcoholic Content of the Brain a Definite Index of the Degree to Which the Subject Is Influenced by the Alcohol?—There have been many arguments for and against this question, mainly because of the well-known fact that the same quantity of alcohol may influence one person and not affect another.

Many workers have tried to prove experimentally what the cause of alcohol tolerance really is. Rosenfield¹⁶ concluded that tolerance was due to more rapid oxidation. Reid Hunt¹⁷ came to the same conclusion from his work on the effect of methylcyanide on animals.

Pringsheim,¹⁸ working with rats and rabbits, found that the alcohol excretion was about the same in habitues as in normal animals. He found that the conjugated sulphuric acid was increased in habitues, but in too small an amount to have any bearing on tolerance. He cites Reid Hunt as having found it to be only 1 per cent of the total. Pringsheim further found that habitues burn up the alcohol much faster (two thirds of the time) than normal animals; that normal animals reach a 66 per

16. Rosenfield: *Einfluss des Alkohols auf den Organismus*, Wiesbaden, 1901.

17. Hunt, Reid: *Public Health Rep. U. S. Mar. Hosp. Serv.*, Washington, bull. 33, 1907.

18. Pringsheim: *Biochem. Ztschr.* **12**:143, 1908.

cent higher alcoholic content in the blood than habitues; that the alcohol in habitues is burned not only in the liver, as it is in normal animals, but also in the heart and in the brain; that normal animals oxidize the same amount of alcohol each hour, while in habitues the oxidation is accelerated each succeeding hour. He found that the organs of both classes contain more alcohol than the blood, but that the ratio $\frac{\text{alcohol in organ}}{\text{alcohol in blood}}$ is much smaller in alcoholic animals because of more intense oxidation. Pringsheim further studied the absorption of alcohol from the gastrointestinal tract. He found that normal animals absorb 20 per cent more alcohol in the first two hours than alcoholic animals do. The greater absorption and the less oxidation are the causes for the alcohol content of the body rising to a higher level in normal animals. During the next four hours he found that the absorption in normal animals decreases to one seventh of the value of the first hour, and he gives this as the explanation for the rapid relative sinking of the alcohol content in normal animals and the prolonged period of absorption, and also the reason for the much longer period that alcohol remains in the body of normal animals. As a result of his extensive study, he concludes that tolerance is, to a great degree, due to increased oxidative powers.

J. Vahlmering¹⁹ found that most of the alcohol is absorbed within the first hour; that it is about equally distributed in the various organs; that the brain receives it more slowly, but finally exceeds the other organs in alcoholic content; and that all of the alcohol is not destroyed or excreted for a long period.

Schweisheimer,²⁰ investigating the alcoholic content of the blood in human alcoholic and normal persons after they had partaken of alcohol, corroborated Pringsheim's results with animals. His results show that the maximum alcohol content is higher in normal persons; that it reaches this maximum in from one and one-half to two hours, remaining at this level for five hours, and then gradually diminishing, while in alcoholic persons it reaches its maximum more quickly, remains at this level for two hours, then subsides much more quickly; he found that normal persons get rid of all the alcohol in seven and one-half hours, while alcoholic persons destroy it in about one half of that time. From his investigation, he concludes that tolerance is due to the decreased maximum alcohol zone, which depends on more rapid oxidation. He also points out that he could find no proof that increased resistance toward alcohol comes into play.

In a later paper, Schweisheimer²¹ brings out an interesting and important point that in chronic alcoholic patients of a decade or more,

19. Vahlmering, J.: *Zentralbl. biochem. Biophys.* **14**:520, 1912.

20. Schweisheimer: *Deutsches Arch. f. klin. Med.* **109**:271, 1912.

21. Schweisheimer: *Schweiz. chem. Ztg.*, 1920, p. 524.

the tissues may lose the previously acquired oxidizing power, and then that such persons may be as much affected by alcohol, if not more, than the abstainer.

The best experimental work to date, therefore, seems to show that alcohol tolerance is due to the ability of the cells to oxidize it rapidly. There is no evidence that an acquired resistance by the cells may be the cause.

In the previous pages, we have summarized our observations as to the alcoholic content of human brains in more than 6,000 persons. Among these, we have had cases of total abstainers, and occasional, mild and habitual drinkers. In the investigation of these cases we have found that the effect produced on all, no matter what habits, is proportional to the amount of alcohol present in the brain. Habitues will be affected just as much as abstainers.

It is true, however, that the same amount of alcohol consumed will affect different persons to a different degree. This, one must remember, is alcohol consumed, and not the quantity of alcohol present in the brain. In those who have a greater tolerance, the power to oxidize alcohol rapidly has been developed to a high degree. They can partake of much more alcohol and show less effect because they destroy it much more quickly. Because of this more rapid oxidation, much of the alcohol consumed is destroyed, and hence it does not accumulate in the brain. The alcohol present in the brain is not proportional to the amount consumed in different persons, because the processes of oxidation in the cells vary. That part of the alcohol, however, which escapes oxidation and hence accumulates in the brain has its effect, and it matters little as to what the alcoholic habits of the person have been.

CONCLUSIONS

1. For the qualitative and quantitative determination of alcohol, the brain is of first importance.
2. The normal alcoholic content of human brain material is less than 0.0025 per cent.
3. The alcoholic content of the brain in persons who have partaken of alcoholic beverage ranges between 0.005 and 0.6 per cent.
4. All patients having an alcoholic content below 0.1 per cent (our designation of "one plus") show no abnormal physiologic effects.
5. Patients with an alcoholic content above 0.1 per cent and up to 0.25 per cent (designated as "two plus") show some physiologic disturbance, as evidenced by increased aggressiveness, and more or less loss of the sense of care. None of these patients, however, shows unbalanced equilibrium, which is commonly called intoxication.

6. When the alcoholic content rises above 0.25 per cent and up to 0.4 per cent (designated as "three plus"), and still higher to 0.6 per cent ("four plus"), the equilibrium of the person becomes unbalanced—a condition generally known as intoxication.

7. The degree to which any person is affected does not depend on the quantity of alcohol consumed, but on the amount of alcohol present in the brain at the time.

Laboratory and Technical Notes

TABLES OF GENERAL APPLICATION FOR VERIFYING COMPLETE COLORIMETRIC CALCULATIONS*

ROBERT F. MCCrackAN, A.M.; KATE E. HARMAN, A.B., AND
EMANUEL PASSAMANECK, B.S., RICHMOND, VA.

It is well known that formulas for colorimetric calculations can be divided into two factors, one of which is constant for any fixed analytic procedure, and the other of which varies with the colorimetric readings. It has been suggested that C^1 represent the constant factor, and that the variable factor be represented by F^2 whether it represents the reading for the known divided by that for the unknown when a colorimeter of the plunger type is used, or the reading for the unknown divided by that for the known when the colorimeter is of the dilution type. Then when W represents the weight of the unknown substance sought

$$FC = W$$

It has been shown that the division necessary to obtain F can be made short, and that repeating decimals can be avoided, by choosing such values as 20, 10 and 25 for the divisors. The purpose of this paper is to explain the use of tables showing values for F , and for W or FC , for all readings to one decimal place between 13.0 and 30.9 when the divisor is 20; between 16.0 and 37.9 when the divisor is 25, and between 6.0 and 15.9 when the divisor is 10. The tables are so much alike in principle that the second alone will be explained.

The second table, which will be most used, probably, is for use only when the unknown is set on 20 for a colorimeter of the plunger type, or the known is 20 in volume for one of the dilution type. The numbers in the first column, marked D , which means dividend, are the integral parts of the colorimeter readings for the dividends that are to be divided by 20, and the fractional parts of the dividends are across the top of the table. In the second column, marked C , meaning constant factors, figures from 1 to 9 are repeated with each whole number found in the first column. Under the fractional parts of the dividends, and opposite 1 of the second column, in each case, the value of F , or of dividend divided by divisor, is found, and under these, opposite the other numbers of the second column are the products of F and C , or W . All values are shown for FC or W , when C is a whole number between 1 and 9. In case C is a decimal fraction between 0.001 and 0.900 with but one significant figure, or a number above 9 with but one

* Paper read before the Meeting of the American Chemical Society, Philadelphia, Sept. 6-10, 1926, Division of Biological Chemistry.

* From the Biochemical Laboratory, Medical College of Virginia.

1. McCrackan, R. F.: A Study of the Mathematics of Colorimetry by Means of a General Formula, *J. Chem. Ed.* **3**:928-931, 1926.

2. McCrackan, R. F.; Passamaneck, E., and Harman, Kate E.: Simplified Calculations in Colorimetry, *J. Chem. Ed.* **3**:416-418, 1926.

significant figure, the figures of the tables still show the values sought, provided that the decimal point is moved correctly in each case. In most procedures the value of *C* contains only one significant figure, but when it contains two figures *W* can still be found by means of the table by pointing off two numbers correctly, and adding them.

While the table can be used in calculations for any fixed colorimetric procedures, Folin's³ well-known methods for analyzing protein-free blood filtrates will be taken to illustrate its use. Let the colorimeter be of the plunger type, the weight of glucose used as the standard be 0.4 mg., and the reading for the known be 19.7, when the unknown is set on 20, to find the number of milligrams of glucose in 100 cc. of blood. The general formula applicable is:

$$\frac{\text{Reading on Known}}{\text{Reading on Unknown}} \times \frac{\text{Vol. Unknown}}{\text{Vol. Known}} \times \frac{\text{Mg. of Standard}}{\text{Vol. Blood Filtrate Analyzed}} \times 1000 = W$$

$$\frac{19.7}{20} \times \frac{25}{25} \times \frac{0.4}{2} \times 1000 = 197$$

A glance at the left member of the equation shows that 19.7/20 is *F*, the variable factor. The balance of the left member of the equation is the constant factor *C* for the analytic procedure, and it equals 200. The significant figure in 200 is 2, and opposite 2 of the second column, under 19.7, the table shows 1.970. To get the correct value for 200, the decimal point must be moved two places to the right. This gives 197 checking the value found by calculation. The value of *F*, or 19.7/20, which is found to be 0.985 by calculation, can be verified by looking under 19.7, opposite 1 of the second column.

The values for *C* in all of Folin's procedures have been calculated and tabulated for use when needed. For his weaker standards they are 4, 30, 15 and 1.5 for uric acid, nonprotein nitrogen, urea nitrogen, and creatinine, respectively. Let the unknowns be set on 20, and let the readings for the knowns in these four determinations be 19.4, 19.6, 20.3 and 20.5, respectively, to find the weights of these substances in 100 cc. of blood. For uric acid, under 19.4, opposite 4 of the second column, the answer 3.88 is found. For nonprotein nitrogen, under 19.6, opposite 3, the figures 2.94 become 29.4, the answer, by moving the point one place. In finding the urea nitrogen, 15, which contains two significant figures, must be used for *C*. The one represents ten, and the five represents units, so opposite 1, under 20.3, the number 1.015 is changed to 10.15 and added to 5.075 found just below, opposite 5 of the second column, giving 15.225 as the unabbreviated answer. Similarly with the creatinine, where *C* is 1.5, the number under 20.5, opposite 1, is 1.025; the number opposite 5, divided by 10, is 0.5125, and the sum of the two numbers is 1.5375, which might be recorded as 1.54 mg.

While calculations, made in the old ways, can be done away with, and these tables used instead, this is not recommended, and particularly not in the work of technicians and students. Calculations should be made independently, and the tables used as a means of checking the arithmetic.

3. Folin, Otto: Laboratory Manual of Biological Chemistry, New York, D. Appleton & Co., 1926, pp. 227-277. Folin, Otto, and Wu, H.: A System of Blood Analysis, J. Biol. Chem. 38:81-110, 1919.

TABLE 1.—Values for Dividends Divided by 10 and Multiplied by from 1 to 9 When Colorimeter Readings Range from 6.0 to 15.9

D C	0.0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
6	1	0.60	0.61	0.62	0.63	0.64	0.65	0.66	0.67	0.68
	2	1.20	1.22	1.24	1.26	1.28	1.30	1.32	1.34	1.36
	3	1.80	1.83	1.86	1.89	1.92	1.95	1.98	2.01	2.04
	4	2.40	2.44	2.48	2.52	2.56	2.60	2.64	2.68	2.72
	5	3.00	3.06	3.10	3.15	3.20	3.25	3.30	3.35	3.40
	6	3.60	3.66	3.72	3.78	3.84	3.90	3.96	4.02	4.08
	7	4.20	4.27	4.34	4.41	4.48	4.55	4.62	4.69	4.76
	8	4.80	4.88	4.96	5.04	5.12	5.20	5.28	5.36	5.44
	9	5.40	5.49	5.58	5.67	5.76	5.85	5.94	6.03	6.12
7	1	0.70	0.71	0.72	0.73	0.74	0.75	0.76	0.77	0.78
	2	1.40	1.42	1.44	1.46	1.48	1.50	1.52	1.54	1.56
	3	2.10	2.13	2.16	2.19	2.22	2.25	2.28	2.31	2.34
	4	2.80	2.84	2.88	2.92	2.96	3.00	3.04	3.08	3.12
	5	3.50	3.55	3.60	3.65	3.70	3.75	3.80	3.85	3.90
	6	4.20	4.26	4.32	4.38	4.44	4.50	4.56	4.62	4.68
	7	4.90	4.97	5.04	5.11	5.18	5.25	5.32	5.39	5.46
	8	5.60	5.68	5.76	5.84	5.92	6.00	6.08	6.16	6.24
	9	6.30	6.39	6.48	6.57	6.66	6.75	6.84	6.93	7.02
8	1	0.80	0.81	0.82	0.83	0.84	0.85	0.86	0.87	0.88
	2	1.60	1.62	1.64	1.66	1.68	1.70	1.72	1.74	1.76
	3	2.40	2.43	2.46	2.49	2.52	2.55	2.58	2.61	2.64
	4	3.20	3.24	3.28	3.32	3.36	3.40	3.44	3.48	3.52
	5	4.00	4.06	4.10	4.15	4.20	4.25	4.30	4.35	4.40
	6	4.80	4.86	4.92	4.98	5.04	5.10	5.16	5.22	5.28
	7	5.60	5.67	5.74	5.81	5.88	5.95	6.02	6.09	6.16
	8	6.40	6.48	6.56	6.64	6.72	6.80	6.88	6.96	7.04
	9	7.20	7.29	7.38	7.47	7.56	7.65	7.74	7.83	7.92
9	1	0.90	0.91	0.92	0.93	0.94	0.95	0.96	0.97	0.98
	2	1.80	1.82	1.84	1.86	1.88	1.90	1.92	1.94	1.96
	3	2.70	2.73	2.76	2.79	2.82	2.85	2.88	2.91	2.94
	4	3.60	3.64	3.68	3.72	3.76	3.80	3.84	3.88	3.92
	5	4.50	4.55	4.60	4.65	4.70	4.75	4.80	4.85	4.90
	6	5.40	5.46	5.52	5.58	5.64	5.70	5.76	5.82	5.88
	7	6.30	6.37	6.44	6.51	6.58	6.65	6.72	6.79	6.86
	8	7.20	7.28	7.36	7.44	7.52	7.60	7.68	7.76	7.84
	9	8.10	8.19	8.28	8.37	8.46	8.55	8.64	8.73	8.82
10	1	1.00	1.01	1.02	1.03	1.04	1.05	1.06	1.07	1.08
	2	2.00	2.02	2.04	2.06	2.08	2.10	2.12	2.14	2.16
	3	3.00	3.03	3.06	3.09	3.12	3.15	3.18	3.21	3.24
	4	4.00	4.04	4.08	4.12	4.16	4.20	4.24	4.28	4.32
	5	5.00	5.05	5.10	5.15	5.20	5.25	5.30	5.35	5.40
	6	6.00	6.06	6.12	6.18	6.24	6.30	6.36	6.42	6.48
	7	7.00	7.07	7.14	7.21	7.28	7.35	7.42	7.49	7.56
	8	8.00	8.08	8.16	8.24	8.32	8.40	8.48	8.56	8.64
	9	9.00	9.09	9.18	9.27	9.36	9.45	9.54	9.63	9.72
11	1	1.10	1.11	1.12	1.13	1.14	1.15	1.16	1.17	1.18
	2	2.20	2.22	2.24	2.26	2.28	2.30	2.32	2.34	2.36
	3	3.30	3.33	3.36	3.39	3.42	3.45	3.48	3.51	3.54
	4	4.40	4.44	4.48	4.52	4.56	4.60	4.64	4.68	4.72
	5	5.50	5.55	5.60	5.65	5.70	5.75	5.80	5.85	5.90
	6	6.60	6.66	6.72	6.78	6.84	6.90	6.96	7.02	7.08
	7	7.70	7.77	7.84	7.91	7.98	8.05	8.12	8.19	8.26
	8	8.80	8.88	8.96	9.04	9.12	9.20	9.28	9.36	9.44
	9	9.90	9.99	10.08	10.17	10.26	10.35	10.44	10.53	10.62
12	1	1.20	1.21	1.22	1.23	1.24	1.25	1.26	1.27	1.28
	2	2.40	2.42	2.44	2.46	2.48	2.50	2.52	2.54	2.56
	3	3.60	3.63	3.66	3.69	3.72	3.75	3.78	3.81	3.84
	4	4.80	4.84	4.88	4.92	4.96	5.00	5.04	5.08	5.12
	5	6.00	6.06	6.10	6.15	6.20	6.25	6.30	6.35	6.40
	6	7.20	7.26	7.32	7.38	7.44	7.50	7.56	7.62	7.68
	7	8.40	8.47	8.54	8.61	8.68	8.75	8.82	8.89	8.96
	8	9.60	9.68	9.76	9.84	9.92	10.00	10.08	10.16	10.24
	9	10.80	10.89	10.98	11.07	11.16	11.25	11.34	11.43	11.52
13	1	1.30	1.31	1.32	1.33	1.34	1.35	1.36	1.37	1.38
	2	2.60	2.62	2.64	2.66	2.68	2.70	2.72	2.74	2.76
	3	3.90	3.93	3.96	3.99	4.02	4.05	4.08	4.11	4.14
	4	5.20	5.24	5.28	5.32	5.36	5.40	5.44	5.48	5.52
	5	6.50	6.55	6.60	6.65	6.70	6.75	6.80	6.85	6.90
	6	7.80	7.86	7.92	7.98	8.04	8.10	8.16	8.22	8.28
	7	9.10	9.17	9.24	9.31	9.38	9.45	9.52	9.59	9.66
	8	10.40	10.48	10.56	10.64	10.72	10.80	10.88	10.96	11.04
	9	11.70	11.79	11.88	11.97	12.06	12.15	12.24	12.33	12.42

TABLE 1.—Values for Dividends Divided by 10 and Multiplied by from 1 to 9 When Colorimeter Readings Range from 6.0 to 15.9—(Continued)

D C	0.0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
14	1	1.40	1.41	1.42	1.43	1.44	1.45	1.46	1.47	1.48
	2	2.80	2.82	2.84	2.86	2.88	2.90	2.92	2.94	2.96
	3	4.20	4.23	4.26	4.29	4.32	4.35	4.38	4.41	4.44
	4	5.60	5.64	5.68	5.72	5.76	5.80	5.84	5.88	5.92
	5	7.00	7.05	7.10	7.15	7.20	7.25	7.30	7.35	7.40
	6	8.40	8.46	8.52	8.58	8.64	8.70	8.76	8.82	8.88
	7	9.80	9.87	9.94	10.01	10.08	10.15	10.22	10.29	10.36
	8	11.20	11.28	11.36	11.44	11.52	11.60	11.68	11.76	11.84
	9	12.60	12.69	12.78	12.87	12.96	13.06	13.14	13.23	13.32
15	1	1.50	1.51	1.52	1.53	1.54	1.55	1.56	1.57	1.58
	2	3.00	3.02	3.04	3.06	3.08	3.10	3.12	3.14	3.16
	3	4.50	4.53	4.56	4.59	4.62	4.65	4.68	4.71	4.74
	4	6.00	6.04	6.08	6.12	6.16	6.20	6.24	6.28	6.32
	5	7.50	7.55	7.60	7.65	7.70	7.75	7.80	7.85	7.90
	6	9.00	9.06	9.12	9.18	9.24	9.30	9.36	9.42	9.48
	7	10.50	10.57	10.64	10.71	10.78	10.85	10.92	10.99	11.06
	8	12.00	12.08	12.16	12.24	12.32	12.40	12.48	12.56	12.64
	9	13.50	13.59	13.68	13.77	13.86	13.95	14.04	14.13	14.22

TABLE 2.—Values for Dividends Divided by 20 and Multiplied by 1 to 9 When Colorimeter Readings Range from 13.0 to 30.9 *

D C	0.0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
13	1	0.650	0.655	0.660	0.665	0.670	0.675	0.680	0.685	0.690
	2	1.300	1.310	1.320	1.330	1.340	1.350	1.360	1.370	1.380
	3	1.950	1.965	1.980	1.995	2.010	2.025	2.040	2.055	2.070
	4	2.600	2.620	2.640	2.660	2.680	2.700	2.720	2.740	2.760
	5	3.250	3.275	3.300	3.325	3.350	3.375	3.400	3.425	3.450
	6	3.900	3.930	3.960	3.990	4.020	4.050	4.080	4.110	4.140
	7	4.550	4.585	4.620	4.655	4.690	4.725	4.760	4.795	4.830
	8	5.200	5.240	5.280	5.320	5.360	5.400	5.440	5.480	5.520
	9	5.850	5.895	5.940	5.985	6.030	6.075	6.120	6.165	6.210
14	1	0.700	0.705	0.710	0.715	0.720	0.725	0.730	0.735	0.740
	2	1.400	1.410	1.420	1.430	1.440	1.450	1.460	1.470	1.480
	3	2.100	2.115	2.130	2.145	2.160	2.175	2.190	2.205	2.220
	4	2.800	2.820	2.840	2.860	2.880	2.900	2.920	2.940	2.960
	5	3.500	3.525	3.550	3.575	3.600	3.625	3.650	3.675	3.700
	6	4.200	4.230	4.260	4.290	4.320	4.350	4.380	4.410	4.440
	7	4.900	4.935	4.970	5.005	5.040	5.075	5.110	5.145	5.180
	8	5.600	5.640	5.680	5.720	5.760	5.800	5.840	5.880	5.920
	9	6.300	6.345	6.390	6.435	6.480	6.525	6.570	6.615	6.660
15	1	0.750	0.755	0.760	0.765	0.770	0.775	0.780	0.785	0.790
	2	1.500	1.510	1.520	1.530	1.540	1.550	1.560	1.570	1.580
	3	2.250	2.265	2.280	2.295	2.310	2.325	2.340	2.355	2.370
	4	3.000	3.020	3.040	3.060	3.080	3.100	3.120	3.140	3.160
	5	3.750	3.775	3.800	3.825	3.850	3.875	3.900	3.925	3.950
	6	4.500	4.530	4.560	4.590	4.620	4.650	4.680	4.710	4.740
	7	5.250	5.285	5.320	5.355	5.390	5.425	5.460	5.495	5.530
	8	6.000	6.040	6.080	6.120	6.160	6.200	6.240	6.280	6.320
	9	6.750	6.795	6.840	6.885	6.930	6.975	7.020	7.065	7.110
16	1	0.800	0.805	0.810	0.815	0.820	0.825	0.830	0.835	0.840
	2	1.600	1.610	1.620	1.630	1.640	1.650	1.660	1.670	1.680
	3	2.400	2.415	2.430	2.445	2.460	2.475	2.490	2.505	2.520
	4	3.200	3.220	3.240	3.260	3.280	3.300	3.320	3.340	3.360
	5	4.000	4.025	4.050	4.075	4.100	4.125	4.150	4.175	4.200
	6	4.800	4.830	4.860	4.890	4.920	4.950	4.980	5.010	5.040
	7	5.600	5.635	5.670	5.705	5.740	5.775	5.810	5.845	5.880
	8	6.400	6.440	6.480	6.520	6.560	6.600	6.640	6.680	6.720
	9	7.200	7.245	7.290	7.335	7.380	7.425	7.470	7.515	7.560
17	1	0.850	0.855	0.860	0.865	0.870	0.875	0.880	0.885	0.890
	2	1.700	1.710	1.720	1.730	1.740	1.750	1.760	1.770	1.780
	3	2.550	2.565	2.580	2.595	2.610	2.625	2.640	2.655	2.670
	4	3.400	3.420	3.440	3.460	3.480	3.500	3.520	3.540	3.560
	5	4.250	4.275	4.300	4.325	4.350	4.375	4.400	4.425	4.450
	6	5.100	5.130	5.160	5.190	5.220	5.250	5.280	5.310	5.340
	7	5.950	5.985	6.020	6.055	6.090	6.125	6.160	6.195	6.230
	8	6.800	6.840	6.880	6.920	6.960	7.000	7.040	7.080	7.120
	9	7.650	7.695	7.740	7.785	7.830	7.875	7.920	7.965	8.010

* The integral parts of the dividends, D, are shown in the first column, and the fractional parts at the top of the page. The constant factors, C, are shown in the second column, and products are opposite them in each case, under the appropriate fractional part of the dividend. Values from 0.001 to 1,000 times as great are obtained by moving the decimal point.

TABLE 2.—Values for Dividends Divided by 20 and Multiplied by 1 to 9 When Colorimeter Readings Range from 13.0 to 30.9—(Continued)

D C	0.0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
18	1	0.900	0.905	0.910	0.915	0.920	0.925	0.930	0.935	0.940
	2	1.800	1.810	1.820	1.830	1.840	1.850	1.860	1.870	1.880
	3	2.700	2.715	2.730	2.745	2.760	2.775	2.790	2.805	2.820
	4	3.600	3.620	3.640	3.660	3.680	3.700	3.720	3.740	3.760
	5	4.500	4.525	4.550	4.575	4.600	4.625	4.650	4.675	4.700
	6	5.400	5.430	5.460	5.490	5.520	5.550	5.580	5.610	5.640
	7	6.300	6.335	6.370	6.405	6.440	6.475	6.510	6.545	6.580
	8	7.200	7.240	7.280	7.320	7.360	7.400	7.440	7.480	7.520
	9	8.100	8.145	8.190	8.235	8.280	8.325	8.370	8.415	8.460
19	1	0.950	0.955	0.960	0.965	0.970	0.975	0.980	0.985	0.990
	2	1.900	1.910	1.920	1.930	1.940	1.950	1.960	1.970	1.980
	3	2.850	2.865	2.880	2.895	2.910	2.925	2.940	2.955	2.970
	4	3.800	3.820	3.840	3.860	3.880	3.900	3.920	3.940	3.960
	5	4.750	4.775	4.800	4.825	4.850	4.875	4.900	4.925	4.950
	6	5.700	5.730	5.760	5.790	5.820	5.850	5.880	5.910	5.940
	7	6.650	6.685	6.720	6.755	6.790	6.825	6.860	6.895	6.930
	8	7.600	7.640	7.680	7.720	7.760	7.800	7.840	7.880	7.920
	9	8.550	8.595	8.640	8.685	8.730	8.775	8.820	8.865	8.910
20	1	1.000	1.005	1.010	1.015	1.020	1.025	1.030	1.035	1.040
	2	2.000	2.010	2.020	2.030	2.040	2.050	2.060	2.070	2.080
	3	3.000	3.015	3.030	3.045	3.060	3.075	3.090	3.105	3.120
	4	4.000	4.020	4.040	4.060	4.080	4.100	4.120	4.140	4.160
	5	5.000	5.025	5.050	5.075	5.100	5.125	5.150	5.175	5.200
	6	6.000	6.030	6.060	6.090	6.120	6.150	6.180	6.210	6.240
	7	7.000	7.035	7.070	7.105	7.140	7.175	7.210	7.245	7.280
	8	8.000	8.040	8.080	8.120	8.160	8.200	8.240	8.280	8.320
	9	9.000	9.045	9.090	9.135	9.180	9.225	9.270	9.315	9.360
21	1	1.050	1.055	1.060	1.065	1.070	1.075	1.080	1.085	1.090
	2	2.100	2.110	2.120	2.130	2.140	2.150	2.160	2.170	2.180
	3	3.150	3.165	3.180	3.195	3.210	3.225	3.240	3.255	3.270
	4	4.200	4.220	4.240	4.260	4.280	4.300	4.320	4.340	4.360
	5	5.250	5.275	5.300	5.325	5.350	5.375	5.400	5.425	5.450
	6	6.300	6.330	6.360	6.390	6.420	6.450	6.480	6.510	6.540
	7	7.350	7.385	7.420	7.455	7.490	7.525	7.560	7.595	7.630
	8	8.400	8.440	8.480	8.520	8.560	8.600	8.640	8.680	8.720
	9	9.450	9.495	9.540	9.585	9.630	9.675	9.720	9.765	9.810
22	1	1.100	1.105	1.110	1.115	1.120	1.125	1.130	1.135	1.140
	2	2.200	2.210	2.220	2.230	2.240	2.250	2.260	2.270	2.280
	3	3.300	3.315	3.330	3.345	3.360	3.375	3.390	3.405	3.420
	4	4.400	4.420	4.440	4.460	4.480	4.500	4.520	4.540	4.560
	5	5.500	5.525	5.550	5.575	5.600	5.625	5.650	5.675	5.700
	6	6.600	6.630	6.660	6.690	6.720	6.750	6.780	6.810	6.840
	7	7.700	7.735	7.770	7.805	7.840	7.875	7.910	7.945	7.980
	8	8.800	8.840	8.880	8.920	8.960	9.000	9.040	9.080	9.120
	9	9.900	9.945	9.990	10.035	10.080	10.125	10.170	10.215	10.260
23	1	1.150	1.155	1.160	1.165	1.170	1.175	1.180	1.185	1.190
	2	2.300	2.310	2.320	2.330	2.340	2.350	2.360	2.370	2.380
	3	3.450	3.465	3.480	3.495	3.510	3.525	3.540	3.555	3.570
	4	4.600	4.620	4.640	4.660	4.680	4.700	4.720	4.740	4.760
	5	5.750	5.775	5.800	5.825	5.850	5.875	5.900	5.925	5.950
	6	6.900	6.930	6.960	6.990	7.020	7.050	7.080	7.110	7.140
	7	8.050	8.085	8.120	8.155	8.190	8.225	8.260	8.295	8.330
	8	9.200	9.240	9.280	9.320	9.360	9.400	9.440	9.480	9.520
	9	10.350	10.395	10.440	10.485	10.530	10.575	10.620	10.665	10.710
24	1	1.200	1.205	1.210	1.215	1.220	1.225	1.230	1.235	1.240
	2	2.400	2.410	2.420	2.430	2.440	2.450	2.460	2.470	2.480
	3	3.600	3.615	3.630	3.645	3.660	3.675	3.690	3.705	3.720
	4	4.800	4.820	4.840	4.860	4.880	4.900	4.920	4.940	4.960
	5	6.000	6.025	6.050	6.075	6.100	6.125	6.150	6.175	6.200
	6	7.200	7.230	7.260	7.290	7.320	7.350	7.380	7.410	7.440
	7	8.400	8.435	8.470	8.505	8.540	8.575	8.610	8.645	8.680
	8	9.600	9.640	9.680	9.720	9.760	9.800	9.840	9.880	9.920
	9	10.800	10.845	10.890	10.935	10.980	11.025	11.070	11.115	11.160
25	1	1.250	1.255	1.260	1.265	1.270	1.275	1.280	1.285	1.290
	2	2.500	2.510	2.520	2.530	2.540	2.550	2.560	2.570	2.580
	3	3.750	3.765	3.780	3.795	3.810	3.825	3.840	3.855	3.870
	4	5.000	5.020	5.040	5.060	5.080	5.100	5.120	5.140	5.160
	5	6.250	6.275	6.300	6.325	6.350	6.375	6.400	6.425	6.450
	6	7.500	7.530	7.560	7.590	7.620	7.650	7.680	7.710	7.740
	7	8.750	8.785	8.820	8.855	8.890	8.925	8.960	8.995	9.030
	8	10.000	10.040	10.080	10.120	10.160	10.200	10.240	10.280	10.320
	9	11.250	11.295	11.340	11.385	11.430	11.475	11.520	11.565	11.610

TABLE 2.—Values for Dividends Divided by 20 and Multiplied by 1 to 9 When Colorimeter Readings Range from 13.0 to 30.9—(Continued)

D O	0.0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
26	1	1.300	1.306	1.310	1.315	1.320	1.325	1.330	1.335	1.340
	2	2.600	2.610	2.620	2.630	2.640	2.650	2.660	2.670	2.680
	3	3.900	3.915	3.930	3.945	3.960	3.975	3.990	4.005	4.020
	4	5.200	5.220	5.240	5.260	5.280	5.300	5.320	5.340	5.360
	5	6.500	6.525	6.550	6.575	6.600	6.625	6.650	6.675	6.700
	6	7.800	7.830	7.860	7.890	7.920	7.950	7.980	8.010	8.040
	7	9.100	9.135	9.170	9.205	9.240	9.275	9.310	9.345	9.380
	8	10.400	10.440	10.480	10.520	10.560	10.600	10.640	10.680	10.720
	9	11.700	11.745	11.790	11.835	11.880	11.925	11.970	12.015	12.060
27	1	1.350	1.355	1.360	1.365	1.370	1.375	1.380	1.385	1.390
	2	2.700	2.710	2.720	2.730	2.740	2.750	2.760	2.770	2.780
	3	4.050	4.065	4.080	4.095	4.110	4.125	4.140	4.155	4.170
	4	5.400	5.420	5.440	5.460	5.480	5.500	5.520	5.540	5.560
	5	6.750	6.775	6.800	6.825	6.850	6.875	6.900	6.925	6.950
	6	8.100	8.130	8.160	8.190	8.220	8.250	8.280	8.310	8.340
	7	9.450	9.485	9.520	9.555	9.590	9.625	9.660	9.695	9.730
	8	10.800	10.840	10.880	10.920	10.960	11.000	11.040	11.080	11.120
	9	12.150	12.195	12.240	12.285	12.330	12.375	12.420	12.465	12.510
28	1	1.400	1.405	1.410	1.415	1.420	1.425	1.430	1.435	1.440
	2	2.800	2.810	2.820	2.830	2.840	2.850	2.860	2.870	2.880
	3	4.200	4.215	4.230	4.245	4.260	4.275	4.290	4.305	4.320
	4	5.600	5.620	5.640	5.660	5.680	5.700	5.720	5.740	5.760
	5	7.000	7.025	7.050	7.075	7.100	7.125	7.150	7.175	7.200
	6	8.400	8.430	8.460	8.490	8.520	8.550	8.580	8.610	8.640
	7	9.800	9.835	9.870	9.905	9.940	9.975	10.010	10.045	10.080
	8	11.200	11.240	11.280	11.320	11.360	11.400	11.440	11.480	11.520
	9	12.600	12.645	12.690	12.735	12.780	12.825	12.870	12.915	12.960
29	1	1.450	1.455	1.460	1.465	1.470	1.475	1.480	1.485	1.490
	2	2.900	2.910	2.920	2.930	2.940	2.950	2.960	2.970	2.980
	3	4.350	4.365	4.380	4.395	4.410	4.425	4.440	4.455	4.470
	4	5.800	5.820	5.840	5.860	5.880	5.900	5.920	5.940	5.960
	5	7.250	7.275	7.300	7.325	7.350	7.375	7.400	7.425	7.450
	6	8.700	8.730	8.760	8.790	8.820	8.850	8.880	8.910	8.940
	7	10.150	10.185	10.220	10.255	10.290	10.325	10.360	10.395	10.430
	8	11.600	11.640	11.680	11.720	11.760	11.800	11.840	11.880	11.920
	9	13.050	13.095	13.140	13.185	13.230	13.275	13.320	13.365	13.410
30	1	1.500	1.505	1.510	1.515	1.520	1.525	1.530	1.535	1.540
	2	3.000	3.010	3.020	3.030	3.040	3.050	3.060	3.070	3.080
	3	4.500	4.515	4.530	4.545	4.560	4.575	4.590	4.605	4.620
	4	6.000	6.020	6.040	6.060	6.080	6.100	6.120	6.140	6.160
	5	7.500	7.525	7.550	7.575	7.600	7.625	7.650	7.675	7.700
	6	9.000	9.030	9.060	9.090	9.120	9.150	9.180	9.210	9.240
	7	10.500	10.535	10.570	10.605	10.640	10.675	10.710	10.745	10.780
	8	12.000	12.040	12.080	12.120	12.160	12.200	12.240	12.280	12.320
	9	13.500	13.545	13.590	13.635	13.680	13.725	13.770	13.815	13.860

TABLE 3.—Values for Dividends Divided by 25 and Multiplied by 1 to 9 When Colorimeter Readings Range from 16.0 to 37.9

D O	0.0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
16	1	0.640	0.644	0.648	0.652	0.656	0.660	0.664	0.668	0.672
	2	1.280	1.288	1.296	1.304	1.312	1.320	1.328	1.336	1.344
	3	1.920	1.932	1.944	1.956	1.968	1.980	1.992	2.004	2.016
	4	2.560	2.576	2.592	2.608	2.624	2.640	2.656	2.672	2.688
	5	3.200	3.220	3.240	3.260	3.280	3.300	3.320	3.340	3.360
	6	3.840	3.864	3.888	3.912	3.936	3.960	3.984	4.008	4.032
	7	4.480	4.508	4.536	4.564	4.592	4.620	4.648	4.676	4.704
	8	5.120	5.152	5.184	5.216	5.248	5.280	5.312	5.344	5.376
	9	5.760	5.796	5.832	5.868	5.904	5.940	5.976	6.012	6.048
17	1	0.680	0.684	0.688	0.692	0.696	0.700	0.704	0.708	0.712
	2	1.360	1.368	1.376	1.384	1.392	1.400	1.408	1.416	1.424
	3	2.040	2.052	2.064	2.076	2.088	2.100	2.112	2.124	2.136
	4	2.720	2.736	2.752	2.768	2.784	2.800	2.816	2.832	2.848
	5	3.400	3.420	3.440	3.460	3.480	3.500	3.520	3.540	3.560
	6	4.080	4.104	4.128	4.152	4.176	4.200	4.224	4.248	4.272
	7	4.760	4.788	4.816	4.844	4.872	4.900	4.928	4.956	4.984
	8	5.440	5.472	5.504	5.536	5.568	5.600	5.632	5.664	5.696
	9	6.120	6.156	6.192	6.228	6.264	6.300	6.336	6.372	6.408

TABLE 3.—Values for Dividends Divided by 25 and Multiplied by 1 to 9 When Colorimeter Readings Range from 16.0 to 37.9—(Continued)

D C	0.0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
18	1	0.720	0.724	0.728	0.732	0.736	0.740	0.744	0.748	0.752
	2	1.440	1.448	1.456	1.464	1.472	1.480	1.488	1.496	1.504
	3	2.160	2.172	2.184	2.196	2.208	2.220	2.232	2.244	2.256
	4	2.880	2.896	2.912	2.928	2.944	2.960	2.976	2.992	3.008
	5	3.600	3.620	3.640	3.660	3.680	3.700	3.720	3.740	3.760
	6	4.320	4.344	4.368	4.392	4.416	4.440	4.464	4.488	4.512
	7	5.040	5.068	5.096	5.124	5.152	5.180	5.208	5.236	5.264
	8	5.760	5.792	5.824	5.856	5.888	5.920	5.952	5.984	6.016
	9	6.480	6.516	6.552	6.588	6.624	6.660	6.696	6.732	6.768
19	1	0.760	0.764	0.768	0.772	0.776	0.780	0.784	0.788	0.792
	2	1.520	1.528	1.536	1.544	1.552	1.560	1.568	1.576	1.584
	3	2.280	2.292	2.304	2.316	2.328	2.340	2.352	2.364	2.376
	4	3.040	3.066	3.072	3.088	3.104	3.120	3.136	3.152	3.168
	5	3.800	3.820	3.840	3.860	3.880	3.900	3.920	3.940	3.960
	6	4.560	4.584	4.608	4.632	4.656	4.680	4.704	4.728	4.752
	7	5.320	5.348	5.376	5.404	5.432	5.460	5.488	5.516	5.544
	8	6.080	6.112	6.144	6.176	6.208	6.240	6.272	6.304	6.336
	9	6.840	6.876	6.912	6.948	6.984	7.020	7.056	7.092	7.128
20	1	0.800	0.804	0.808	0.812	0.816	0.820	0.824	0.828	0.832
	2	1.600	1.608	1.616	1.624	1.632	1.640	1.648	1.656	1.664
	3	2.400	2.412	2.424	2.436	2.448	2.460	2.472	2.484	2.496
	4	3.200	3.216	3.232	3.248	3.264	3.280	3.296	3.312	3.328
	5	4.000	4.020	4.040	4.060	4.080	4.100	4.120	4.140	4.160
	6	4.800	4.824	4.848	4.872	4.896	4.920	4.944	4.968	4.992
	7	5.600	5.628	5.656	5.684	5.712	5.740	5.768	5.796	5.824
	8	6.400	6.432	6.464	6.496	6.528	6.560	6.592	6.624	6.656
	9	7.200	7.236	7.272	7.308	7.344	7.380	7.416	7.452	7.488
21	1	0.840	0.844	0.848	0.852	0.856	0.860	0.864	0.868	0.872
	2	1.680	1.688	1.696	1.704	1.712	1.720	1.728	1.736	1.744
	3	2.520	2.532	2.544	2.556	2.568	2.580	2.592	2.604	2.616
	4	3.360	3.376	3.392	3.408	3.424	3.440	3.456	3.472	3.488
	5	4.200	4.220	4.240	4.260	4.280	4.300	4.320	4.340	4.360
	6	5.040	5.064	5.088	5.112	5.136	5.160	5.184	5.208	5.232
	7	5.880	5.908	5.936	5.964	5.992	6.020	6.048	6.076	6.104
	8	6.720	6.752	6.784	6.816	6.848	6.880	6.912	6.944	6.976
	9	7.560	7.596	7.632	7.668	7.704	7.740	7.776	7.812	7.848
22	1	0.880	0.884	0.888	0.892	0.896	0.900	0.904	0.908	0.912
	2	1.760	1.768	1.776	1.784	1.792	1.800	1.808	1.816	1.824
	3	2.640	2.652	2.664	2.676	2.688	2.700	2.712	2.724	2.736
	4	3.520	3.536	3.552	3.568	3.584	3.600	3.616	3.632	3.648
	5	4.400	4.420	4.440	4.460	4.480	4.500	4.520	4.540	4.560
	6	5.280	5.304	5.328	5.352	5.376	5.400	5.424	5.448	5.472
	7	6.160	6.188	6.216	6.244	6.272	6.300	6.328	6.356	6.384
	8	7.040	7.072	7.104	7.136	7.168	7.200	7.232	7.264	7.296
	9	7.920	7.956	7.992	8.028	8.064	8.100	8.136	8.172	8.208
23	1	0.920	0.924	0.928	0.932	0.936	0.940	0.944	0.948	0.952
	2	1.840	1.848	1.856	1.864	1.872	1.880	1.888	1.896	1.904
	3	2.760	2.772	2.784	2.796	2.808	2.820	2.832	2.844	2.856
	4	3.680	3.696	3.712	3.728	3.744	3.760	3.776	3.792	3.808
	5	4.600	4.620	4.640	4.660	4.680	4.700	4.720	4.740	4.760
	6	5.520	5.544	5.568	5.592	5.616	5.640	5.664	5.688	5.712
	7	6.440	6.468	6.496	6.524	6.552	6.580	6.608	6.636	6.664
	8	7.360	7.392	7.424	7.456	7.488	7.520	7.552	7.584	7.616
	9	8.280	8.316	8.352	8.388	8.424	8.460	8.496	8.532	8.568
24	1	0.960	0.964	0.968	0.972	0.976	0.980	0.984	0.988	0.992
	2	1.920	1.928	1.936	1.944	1.952	1.960	1.968	1.976	1.984
	3	2.880	2.892	2.904	2.916	2.928	2.940	2.952	2.964	2.976
	4	3.840	3.856	3.872	3.888	3.904	3.920	3.936	3.952	3.968
	5	4.800	4.820	4.840	4.860	4.880	4.900	4.920	4.940	4.960
	6	5.760	5.784	5.808	5.832	5.856	5.880	5.904	5.928	5.952
	7	6.720	6.748	6.776	6.804	6.832	6.860	6.888	6.916	6.944
	8	7.680	7.712	7.744	7.776	7.808	7.840	7.872	7.904	7.936
	9	8.640	8.676	8.712	8.748	8.784	8.820	8.856	8.892	8.928
25	1	1.000	1.004	1.008	1.012	1.016	1.020	1.024	1.028	1.032
	2	2.000	2.008	2.016	2.024	2.032	2.040	2.048	2.056	2.064
	3	3.000	3.012	3.024	3.036	3.048	3.060	3.072	3.084	3.096
	4	4.000	4.016	4.032	4.048	4.064	4.080	4.096	4.112	4.128
	5	5.000	5.020	5.040	5.060	5.080	5.100	5.120	5.140	5.160
	6	6.000	6.024	6.048	6.072	6.096	6.120	6.144	6.168	6.192
	7	7.000	7.028	7.056	7.084	7.112	7.140	7.168	7.196	7.224
	8	8.000	8.032	8.064	8.096	8.128	8.160	8.192	8.224	8.256
	9	9.000	9.036	9.072	9.108	9.144	9.180	9.216	9.252	9.288

TABLE 3.—Values for Dividends Divided by 25 and Multiplied by 1 to 9 When Colorimeter Readings Range from 16.0 to 37.9—(Continued)

D C	0.0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
26	1	1.040	1.044	1.048	1.052	1.056	1.060	1.064	1.068	1.072
	2	2.080	2.088	2.096	2.104	2.112	2.120	2.128	2.136	2.144
	3	3.120	3.132	3.144	3.156	3.168	3.180	3.192	3.204	3.216
	4	4.160	4.176	4.192	4.208	4.224	4.240	4.256	4.272	4.288
	5	5.200	5.220	5.240	5.260	5.280	5.300	5.320	5.340	5.360
	6	6.240	6.264	6.288	6.312	6.336	6.360	6.384	6.408	6.432
	7	7.280	7.308	7.336	7.364	7.392	7.420	7.448	7.476	7.504
	8	8.320	8.352	8.384	8.416	8.448	8.480	8.512	8.544	8.576
	9	9.360	9.396	9.432	9.468	9.504	9.540	9.576	9.612	9.648
27	1	1.080	1.084	1.088	1.092	1.096	1.100	1.104	1.108	1.112
	2	2.160	2.168	2.176	2.184	2.192	2.200	2.208	2.216	2.224
	3	3.240	3.252	3.264	3.276	3.288	3.300	3.312	3.324	3.336
	4	4.320	4.336	4.352	4.368	4.384	4.400	4.416	4.432	4.448
	5	5.400	5.420	5.440	5.460	5.480	5.500	5.520	5.540	5.560
	6	6.480	6.504	6.528	6.552	6.576	6.600	6.624	6.648	6.672
	7	7.560	7.588	7.616	7.644	7.672	7.700	7.728	7.756	7.784
	8	8.640	8.672	8.704	8.736	8.768	8.800	8.832	8.864	8.896
	9	9.720	9.756	9.792	9.828	9.864	9.900	9.936	9.972	10.008
28	1	1.120	1.124	1.128	1.132	1.136	1.140	1.144	1.148	1.152
	2	2.240	2.248	2.256	2.264	2.272	2.280	2.288	2.296	2.304
	3	3.360	3.372	3.384	3.396	3.408	3.420	3.432	3.444	3.456
	4	4.480	4.496	4.512	4.528	4.544	4.560	4.576	4.592	4.608
	5	5.600	5.620	5.640	5.660	5.680	5.700	5.720	5.740	5.760
	6	6.720	6.744	6.768	6.792	6.816	6.840	6.864	6.888	6.912
	7	7.840	7.868	7.896	7.924	7.952	7.980	8.008	8.036	8.064
	8	8.960	8.992	9.024	9.056	9.088	9.120	9.152	9.184	9.216
	9	10.080	10.116	10.152	10.188	10.224	10.260	10.296	10.332	10.368
29	1	1.160	1.164	1.168	1.172	1.176	1.180	1.184	1.188	1.192
	2	2.320	2.328	2.336	2.344	2.352	2.360	2.368	2.376	2.384
	3	3.480	3.492	3.504	3.516	3.528	3.540	3.552	3.564	3.576
	4	4.640	4.656	4.672	4.688	4.704	4.720	4.736	4.752	4.768
	5	5.800	5.820	5.840	5.860	5.880	5.900	5.920	5.940	5.960
	6	6.960	6.984	7.008	7.032	7.056	7.080	7.104	7.128	7.152
	7	8.120	8.148	8.176	8.204	8.232	8.260	8.288	8.316	8.344
	8	9.280	9.312	9.344	9.376	9.408	9.440	9.472	9.504	9.536
	9	10.440	10.476	10.512	10.548	10.584	10.620	10.656	10.692	10.728
30	1	1.200	1.204	1.208	1.212	1.216	1.220	1.224	1.228	1.232
	2	2.400	2.408	2.416	2.424	2.432	2.440	2.448	2.456	2.464
	3	3.600	3.612	3.624	3.636	3.648	3.660	3.672	3.684	3.696
	4	4.800	4.816	4.832	4.848	4.864	4.880	4.896	4.912	4.928
	5	6.000	6.020	6.040	6.060	6.080	6.100	6.120	6.140	6.160
	6	7.200	7.224	7.248	7.272	7.296	7.320	7.344	7.368	7.392
	7	8.400	8.428	8.456	8.484	8.512	8.540	8.568	8.596	8.624
	8	9.600	9.632	9.664	9.696	9.728	9.760	9.792	9.824	9.856
	9	10.800	10.836	10.872	10.908	10.944	10.980	11.016	11.052	11.088
31	1	1.240	1.244	1.248	1.252	1.256	1.260	1.264	1.268	1.272
	2	2.480	2.488	2.496	2.504	2.512	2.520	2.528	2.536	2.544
	3	3.720	3.732	3.744	3.756	3.768	3.780	3.792	3.804	3.816
	4	4.960	4.976	4.992	5.008	5.024	5.040	5.056	5.072	5.088
	5	6.200	6.220	6.240	6.260	6.280	6.300	6.320	6.340	6.360
	6	7.440	7.464	7.488	7.512	7.536	7.560	7.584	7.608	7.632
	7	8.680	8.708	8.736	8.764	8.792	8.820	8.848	8.876	8.904
	8	9.920	9.952	9.984	10.016	10.048	10.080	10.112	10.144	10.176
	9	11.160	11.196	11.232	11.268	11.304	11.340	11.376	11.412	11.448
32	1	1.280	1.284	1.288	1.292	1.296	1.300	1.304	1.308	1.312
	2	2.560	2.568	2.576	2.584	2.592	2.600	2.608	2.616	2.624
	3	3.840	3.852	3.864	3.876	3.888	3.900	3.912	3.924	3.936
	4	5.120	5.136	5.152	5.168	5.184	5.200	5.216	5.232	5.248
	5	6.400	6.420	6.440	6.460	6.480	6.500	6.520	6.540	6.560
	6	7.680	7.704	7.728	7.752	7.776	7.800	7.824	7.848	7.872
	7	8.960	8.988	9.016	9.044	9.072	9.100	9.128	9.156	9.184
	8	10.240	10.272	10.304	10.336	10.368	10.400	10.432	10.464	10.496
	9	11.520	11.556	11.592	11.628	11.664	11.700	11.736	11.772	11.808
33	1	1.320	1.324	1.328	1.332	1.336	1.340	1.344	1.348	1.352
	2	2.640	2.648	2.656	2.664	2.672	2.680	2.688	2.696	2.704
	3	3.960	3.972	3.984	3.996	4.008	4.020	4.032	4.044	4.056
	4	5.280	5.296	5.312	5.328	5.344	5.360	5.376	5.392	5.408
	5	6.600	6.620	6.640	6.660	6.680	6.700	6.720	6.740	6.760
	6	7.920	7.944	7.968	7.992	8.016	8.040	8.064	8.088	8.112
	7	9.240	9.268	9.296	9.324	9.352	9.380	9.408	9.436	9.464
	8	10.560	10.592	10.624	10.656	10.688	10.720	10.752	10.784	10.816
	9	11.880	11.916	11.952	11.988	12.024	12.060	12.096	12.132	12.168

TABLE 3.—Values for Dividends Divided by 25 and Multiplied by 1 to 9 When Colorimeter Readings Range from 16.0 to 37.9—(Continued)

D O	0.0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
34	1	1.300	1.364	1.368	1.372	1.376	1.380	1.384	1.388	1.392
	2	2.720	2.728	2.736	2.744	2.752	2.760	2.768	2.776	2.784
	3	4.080	4.092	4.104	4.116	4.128	4.140	4.152	4.164	4.176
	4	5.440	5.456	5.472	5.488	5.504	5.520	5.536	5.552	5.568
	5	6.800	6.820	6.840	6.860	6.880	6.900	6.920	6.940	6.960
	6	8.160	8.184	8.208	8.232	8.256	8.280	8.304	8.328	8.352
	7	9.520	9.548	9.576	9.604	9.632	9.660	9.688	9.716	9.744
	8	10.880	10.912	10.944	10.976	11.008	11.040	11.072	11.104	11.136
	9	12.240	12.276	12.312	12.348	12.384	12.420	12.456	12.492	12.528
25	1	1.400	1.404	1.408	1.412	1.416	1.420	1.424	1.428	1.432
	2	2.800	2.808	2.816	2.824	2.832	2.840	2.848	2.856	2.864
	3	4.200	4.212	4.224	4.236	4.248	4.260	4.272	4.284	4.296
	4	5.600	5.616	5.632	5.648	5.664	5.680	5.696	5.712	5.728
	5	7.000	7.020	7.040	7.060	7.080	7.100	7.120	7.140	7.160
	6	8.400	8.424	8.448	8.472	8.496	8.520	8.544	8.568	8.592
	7	9.800	9.828	9.856	9.884	9.912	9.940	9.968	9.996	10.024
	8	11.200	11.232	11.264	11.296	11.328	11.360	11.392	11.424	11.456
	9	12.600	12.636	12.672	12.708	12.744	12.780	12.816	12.852	12.888
36	1	1.440	1.444	1.448	1.452	1.456	1.460	1.464	1.468	1.472
	2	2.880	2.888	2.896	2.904	2.912	2.920	2.928	2.936	2.944
	3	4.320	4.332	4.344	4.356	4.368	4.380	4.392	4.404	4.416
	4	5.760	5.776	5.792	5.808	5.824	5.840	5.856	5.872	5.888
	5	7.200	7.220	7.240	7.260	7.280	7.300	7.320	7.340	7.360
	6	8.640	8.664	8.688	8.712	8.736	8.760	8.784	8.808	8.832
	7	10.080	10.108	10.136	10.164	10.192	10.220	10.248	10.276	10.304
	8	11.520	11.552	11.584	11.616	11.648	11.680	11.712	11.744	11.776
	9	12.960	12.996	13.032	13.068	13.104	13.140	13.176	13.212	13.248
37	1	1.480	1.484	1.488	1.492	1.496	1.500	1.504	1.508	1.512
	2	2.960	2.968	2.976	2.984	2.992	3.000	3.008	3.016	3.024
	3	4.440	4.452	4.464	4.476	4.488	4.500	4.512	4.524	4.536
	4	5.920	5.936	5.952	5.968	5.984	6.000	6.016	6.032	6.048
	5	7.400	7.420	7.440	7.460	7.480	7.500	7.520	7.540	7.560
	6	8.880	8.904	8.928	8.952	8.976	9.000	9.024	9.048	9.072
	7	10.360	10.388	10.416	10.444	10.472	10.500	10.528	10.556	10.584
	8	11.840	11.872	11.904	11.936	11.968	12.000	12.032	12.064	12.096
	9	13.320	13.356	13.392	13.428	13.464	13.500	13.536	13.572	13.608

SUMMARY

1. Attention has been called to the fact that the answers usually sought in colorimetric calculations are the products of two factors, one of which is constant for any fixed analytic procedure, and the other of which may vary with each analysis.

2. Tables have been explained showing: (a) values for the variable factors obtained by dividing colorimeter readings by colorimeter readings when the divisors are made to equal 20, 25 and 10; (b) the products of the variable and constant factors.

3. The tables are recommended for use in checking colorimetric calculations rather than as a substitute for them.

TECHNIC OF EXAMINATION OF FECES FOR AMEBAS AND OTHER INTESTINAL PROTOZOA

HENRY ALBERT, M.D., RENO, NEV.

Director State Hygienic Laboratory, University of Nevada

The following methods of examining feces for protozoa are the ones used in the State Hygienic Laboratory, University of Nevada. They are based on the methods of Kofoid,¹ and have been found satisfactory.

1. Kofoid, C. A.; Kornhauser, S. I., and Swezy, O.: Criteria for Distinguishing the Endamoeba of Amebiasis from Other Organisms, Arch. Int. Med. **24**:35-50 (July) 1919. Kofoid, C. A.: Amoeba and Man, Univ. Cal. Bull., 1923.

THE TWO METHODS EMPLOYED

1. *Iodine-Eosin Stain of Fresh Material.*—A drop of physiologic sodium chloride solution and one of iodine-eosin stain are placed near together on a slide, but not touching. A round applicator stick or a toothpick is smeared with the feces, and rolled in the drop of physiologic sodium chloride solution and then in the drop of iodine-eosin. A single cover-slip is placed on both drops, half the material under it being stained and the other half unstained. The unstained portion should be examined first for living flagellates and active amebas. In the stained portion the protozoan cysts stand out as bright spherules against the pink background and soon become tinged with the iodine to varying tones of yellow, with the nuclei becoming clearly defined as the iodine penetrates. If glycogen is present in the cysts, it becomes light or dark brown.

Iodine-eosin stain consists of: saturated aqueous solution of eosin in physiologic sodium chloride solution, 2 parts; 5 per cent solution of potassium iodide in physiologic sodium chloride solution saturated with iodine, 1 part; physiologic sodium chloride solution, 2 parts.

The proportion of iodine solution used may be modified to advantage by adding a slight excess of that given in the formula, if the nuclei do not appear after a few moments' application of the stain. The stain should be made up each day from the stock ingredients.

If no bright spherules stand out against the pink background or no other evidence of protozoa is found in two preparations examined, the specimen is reported as negative. If bright spherules (cysts) or living protozoa in the vegetative stage are found, several smears are made and stained with hematoxylin, using the following method:

2. *Hematoxylin Stain of Fixed Material.*—A smear is made on a slide which has previously been thoroughly cleaned in alcohol-ether and flamed. If the fecal material is too dry, it should be moistened slightly with physiologic sodium chloride solution and a thin smear made with the applicator stick or the flat side of a toothpick or by using the edge of another slide or a cover-slip. It should then be immersed directly in Schaudinn's fixing fluid without allowing the slide to become dry. The following steps are used in fixing and staining the preparation:

Schaudinn's fluid¹ (freshly prepared each time) is heated to from 56 to 60 C. for 10 minutes.

70 per cent alcohol tinged with Gram's iodine.....	5 minutes
70 per cent alcohol	5 minutes
50 per cent alcohol	5 minutes
Tap water	2 minutes
2 per cent iron alum* aqueous solution.....	5-12 hours
or heated to 30 C.....	10 minutes-1 hour
Tap water—rinse	1 minute
5 per cent hematoxylin† aqueous solution.....	12-18 hours
or heated to 30 C.....	10 minutes-1 hour
Tap water	1 minute

2. Schaudinn's fluid—2 parts saturated aqueous mercuric chloride in physiologic sodium chloride solution, 1 part absolute or 95 per cent alcohol; 4 cc. glacial acetic acid is added to 96 cc. of the mixture on using.

*Use only violet crystals of iron alum. Reject yellowish powder.

†Use American hematoxylin, standardized white crystals only.

Differentiate ‡ in 1 or 2 per cent iron alum with careful watching under microscope. (After placing in alum solution about a minute, wash in water, then make trial examination.) Wash in running water	10 minutes
50 per cent alcohol	10 minutes
70 per cent alcohol	5 minutes
90 per cent alcohol	5 minutes
100 per cent alcohol	5 minutes
Xylol	5 minutes

The preparation is then mounted in balsam and covered. Examination is made preferably with a binocular microscope using the oil immersion lens.

For the recognition of the several types of protozoa and their differentiation from various forms of vegetable cells, reference must be made to standard texts on protozoology and more especially to the special articles as given in the references.³

‡ Use 4 mm. objective of microscope. Reduce volume of light by lowering substage condenser. If cysts can be found, decolorize until outlines of nuclei become fairly definite. Do not allow preparation to become dry.

3. Boeck, W. C., and Stiles, C. W.: Studies on Various Intestinal Parasites (Especially Amoebae) of Man, Hyg. Lab. Bull., no. 133, U. S. Pub. Health Serv., 1923.

A NEW GLASS CHAMBER FOR THE SCHULTZ-DALE UTERINE STRIP METHOD*

JULIAN H. LEWIS, M.D., PH.D., CHICAGO

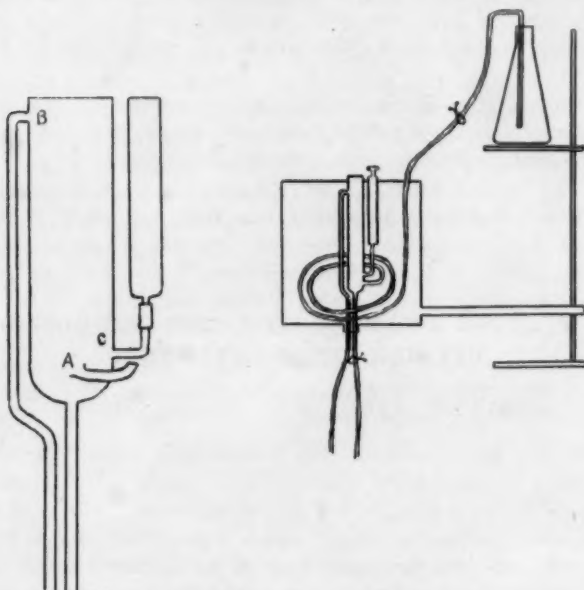
Those who have had experience with Schultz-Dale technic for uterine strip contractions have recognized the importance of constancy of temperature and oxygen supply in obtaining accurate and consistent results. With a glass stopcock or a sensitive needle valve, the oxygen supply is relatively easy to regulate and supply at an even rate; but the temperature of the Locke's solution surrounding the uterine strip is difficult to keep constant with the apparatus as described by Dale.¹ In order to change the solution and wash the preparation when this apparatus is used it is necessary to drain the chamber completely and to fill it through an inlet located outside the water bath. This removal of fluid from around the strip, although temporary, permits a slight desiccation and a marked change in temperature, which often produces a severe spasm of the uterine muscle and a delay in the experiment while awaiting the return of normal conditions. Test solutions introduced into the chamber are necessarily at a different temperature, and, if in considerable amounts, will change the temperature enough to influence the tonus of the uterine musculature.

A modification of the Dale apparatus has been devised which reduces to a minimum changes in temperature due to manipulations during the course of the experiment.

*From the Otho S. A. Sprague Memorial Institute and the Department of Pathology, University of Chicago.

1. Dale: J. Pharmacol. & Exper. Therap. 4:75, 1912.

The glass chamber, of any size desired, is made with three openings in addition to the one at the bottom as may be seen in the illustration. At *A* is an opening of a glass tube near the bottom. To this is attached a piece of rubber tubing 4 or 5 feet (122 or 152 cm.) in length. The rubber tubing is coiled around the glass chamber in the water bath and ends in the supply bottle placed at a level higher than the apparatus. At *B*, as near the top of the chamber as possible, is another opening of a glass tube which is bent downward, parallel to the side of the chamber, and passes through the rubber stopper along with the stem of the chamber. To change the solution in the chamber and wash the uterus strip, the pinch clamp is opened on the rubber tubing going to *A*. The Locke's solution, as it flows through the long rubber tubing, is brought to the same temperature as that of the water bath and the solution in the chamber. The solution enters the chamber at the bottom and forces the old fluid out



New glass chamber for the Schultz-Dale uterine strip method.

through the overflow tube at *B*. As this is done, no change in the tonus of the uterus strip is observed as there is no change in temperature and the new solution is oxygenated as fast as it flows in. The stream of Locke's solution can be allowed to run, without any disturbance, until one is sure that all traces of the old fluid have been removed. The portion below *A* can be removed by opening the stem at the chamber for a moment. As the renewed fluid is warmed while it flows through the rubber tubing, it is not necessary to warm that in the supply bottle much over the temperature of the room, thus minimizing the loss of carbon dioxide from the Locke's solution.

At *C* is another opening with a short piece of glass tubing turned up. To this is attached by means of a short length of heavy rubber tubing a glass syringe whose top is at the same level as the top of the chamber. A solution to be added to the chamber for the purpose of studying its action on the uterus strip is introduced into the syringe, and when enough time has elapsed to bring

it to the temperature of the water bath it is forced into the chamber with the plunger. All the solution can be washed out of the syringe by drawing a fluid back into it and returning it to the chamber.

The apparatus is easy to make, is durable and is easy to clean.

EXPERIMENTS WITH CELLOPHANE AS A STERILIZABLE DIALYZABLE MEMBRANE*

FREDA L. WILSON, M.A., VANCOUVER, CANADA

Instructor in Bacteriology in the University of British Columbia

In a previous article¹ on this subject, it was shown that cellophane may be sterilized in the autoclave at 15 pounds (7 Kg.) pressure for twenty minutes and its dialyzing powers for certain chemicals remain perfect.

Further experiments with cellophane were carried out in the following manner:

TECHNIC

1. A slight depression is made around the end of a 4 inch (10 cm.) length of glass tubing.
2. A piece of cellophane 10 inches (25 cm.) in diameter is folded so that the whole resembles a closed umbrella.
3. The cellophane is fastened around the depression in the tube with Du Pont's household cement and strong thread.
4. A cover for the umbrella is made from a piece of cellophane. The seam is fastened with the cement. (This prevents the bag from spreading when the liquid is put into it.)
5. A small quantity of cotton wool is wrapped around the top of the umbrella-tube, and it is suspended by this means in a large test tube, so that the bottom of the bag is about 1 inch (2.5 cm.) above the bottom of the tube.
6. The umbrella-tube is then plugged with cotton and the whole sterilized for twenty minutes at 15 pounds (7 Kg.) pressure.
7. When cool, 5 cc. of sterile broth is pipetted into the umbrella-tube and 5 cc. of sterile broth into the outside tube.
8. The broth in the umbrella-tube is inoculated.

A series of such tubes were prepared and inoculated with *Staphylococcus aureus* and incubated at 37 C. After twenty-four hours the umbrella-tube cultures showed abundant growth and the broth in the outside tubes remained sterile. The cultures were observed weekly for four weeks and the broth on the outside of the bags remained sterile except in a few cases.

Motile organisms were experimented with but these invariably grew through the cellophane, as the broth in the outside tubes showed growth.

Various methods were tried before the foregoing process was determined apparently to be the most uniformly successful and practical.

* Cellophane, a proprietary material, obviously some modification of cellulose, advertised particularly for the purpose of wrapping food products, is manufactured by the DuPont Cellophane Company of Buffalo.

1. Hill: Vancouver M. A. Bull. 2:10 (Feb.) 1926.

General Review

THE RELATION BETWEEN THE HISTOLOGIC PICTURE AND PROGNOSIS OF TUMORS *

ALFRED PLAUT, M.D.

NEW YORK

The problem of histologic prognosis in tumors is neither new nor old. From the beginning of the microscopic era, the tissue experts, from their observations of the slides, naturally have formed an opinion concerning the progress of the disease. So far the problem is old. But only recently standardization of histologic or even cytologic diagnosis has been attempted. Thus a review of the subject must deal with old as well as with recent literature.

We are faced with problems, not with facts; hence I have made a theoretical, critical and personal review. It is not my purpose to emphasize mistakes in arrangement or interpretation of statistics; but some criticism of this kind can not be avoided. Since my aim is to give a practical presentation, I can and must limit the scope of the investigation. I shall not endeavor to cover the whole field of neoplastic disease in man and animals, and I shall avoid the realm of experimental cancer. Even among the clinically important tumors of man, I shall choose a few of special importance.

Among the many questions on the subject, the following seem prominent:

Are there general criteria indicating in the microscopic picture the degree of clinical malignancy in carcinoma? If not, do such criteria exist for smaller groups of tumors, for example, adenocarcinoma or squamous cell carcinoma?

Is such an estimation possible for the tumors of a single organ?

Can this estimation be made for a certain tumor in a certain organ, for instance, carcinoma of the cervix uteri? This question contains the problem of greatest clinical interest.

Further, I shall discuss single histologic features, such as type of cell, lymphocytic infiltration, etc., in their importance for prognosis. Finally, it may be unavoidable to enter on some discussion of the term malignancy. For technical reasons, the review will not be divided into chapters according to the problems mentioned.

In a few classical sentences Rudolf Virchow has formulated his opinion on what we call today histologic prognosis.

* From the pathologic department of the Woman's Hospital.

One must consider individual cases, and one must never lose sight of the fact that malignancy [in sarcoma] cannot be decided on according to any fixed rule. One must always take into account the individual as well as the organ involved. The experience gained in one case is often wholly fallacious in forming judgment in another case, and general rules on malignancy exist only for medullary sarcomas . . . (p. 268).

I quote this general statement on sarcoma because it shows Virchow's attitude concerning standardized rules.¹ He was also aware of the danger in mixing practice and theory, as his statement in the preface to his oncology shows (page vii), "I have described the prognosis following empiric results exclusively, and I have clearly separated my theoretical interpretations from those based on empiric results." Such a definite separation can scarcely be made at the present time. After dwelling on some general features which he believes must be considered in deciding the malignancy of tumors, Virchow concludes that he has nothing more to say about these questions in general. Thus in Virchow's book no chapter deals in a positive way with histologic prognosis.

The beginning of histologic prognosis was the addition of the term "anaplasia" to the medical vocabulary by Hansemann. He differentiates sharply between three kinds of cells: embryonic cells, young cells and anaplastic cells. According to his definition, anaplastic cells have lost some of their differentiating features; they have been more highly differentiated than they are now.² Hansemann thinks that these cells have retraced the steps of their development; but that this has not resulted in a similarity between anaplastic cells and embryonic cells. The prognostic value of anaplasia has been estimated differently by Hansemann in different publications. He denies (page 92) that the degree of anaplasia is identical with the degree of malignancy. He does not admit the conclusion that the more anaplastic a tumor is, the more easily does metastasis occur. He even claims that such a conclusion would be practically without value, since the degree of anaplasia might change at any time, and frequently does change. A tumor exhibiting slight anaplasia might have a recurrence which is highly anaplastic.

What Hansemann wrote nine years later sounds very different. . . . "Tumors disseminated through the body show a high degree of anaplasia; those of unusual local growth without dissemination have little anaplasia. There are only rare exceptions to this law. Theoretically, then, I could take it for granted that the greater the anaplasia the greater the tendency to form metastases" (page 254).

1. One wonders whether Virchow has expressed a general opinion on histologic prognosis in carcinoma.

2. Did Hansemann mean that the cell itself has changed, or did he mean that the mother cell has had a higher degree of differentiation? How long does the individual cancer cell live?

Hansemann followed up some of his cases. In nearly all cases in which the excised tumor had been highly anaplastic, recurrences and metastases took place; but when the tumor was slightly anaplastic, either there was no recurrence or metastasis, or they were found and showed a higher degree of anaplasia than the primary tumor, even a very high degree. "But it is impossible to tell what makes a tumor more anaplastic, and thus prognosis in all cases of this kind is doubtful. A high degree of anaplasia here too is a better indicator than a slight degree or than its absence" (page 254). This is one of the vital points of the whole problem; histologic prognosis is at its best in cases with definite histologic features, as, for instance, a very high degree of anaplasia. These cases are in the minority, and prognosis based on anaplasia cannot be made efficiently in the average case. In spite of such restrictions, which were realized to a certain extent by Hansemann himself, the term anaplasia has been widely used since whenever the cells of a tumor look unusual. Ribbert has criticized the use or abuse of the word anaplasia.

This word has been widely adopted. But such words taken from an old language very easily assume something dogmatic. A definite opinion is fixed in them. Then they are used everywhere, but people do not realize in each instance what the word means. And, even worse, they are used as explanation of the phenomena from which they are deduced. One does not say any more: The cancer cells are anaplastic, but one takes the anaplasia for the basis of the malignancy. This is the disadvantage of such words.

Adami states that for prognosis one must bear in mind the adult type of the cell in any particular case of tumor in order to estimate correctly the deviation of the tumor cell from the adult type (page 670). This sounds obvious and hardly worth while insisting on, but it reveals pitfalls for prognosis. The outstanding example is carcinoma of the skin. There is hardly any doubt that the cornified squamous cell carcinoma is more malignant than the basal cell carcinoma. However, we are accustomed to regard the prickle cell as the adult differentiated form in the epithelium. The basal cells, as the name *stratum germinativum* indicates, are supposed to be chiefly vegetative, proliferation being their essential function. This severe flaw in our theories of malignancy not only never has been explained satisfactorily, but it even is not realized by many authors who deal with cancer problems. Consequently, tumors of other organs (upper digestive tract, cervix uteri) which are similar to basal cell carcinoma are considered less malignant by some, because they identify them with the basal cell carcinoma of the skin; others, however, believe that these tumors are more malignant because they are composed of less mature cells. As general laws concerning the relation between cell maturity and degree of malignancy are not much

avored this disagreement will probably not be settled soon. But we might ask whether it is safe to regard the basal cells of the skin as not highly differentiated. The skin has functions in metabolism, in immunity reactions; hence that layer of skin which is next to the cutis must have complicated functions even if we cannot see a corresponding structure. In the higher differentiation of a tumor, the architecture is important also. The slowly growing basal cell cancers of the skin frequently show one character which we may explain in a new way from the architectural standpoint. The borderline of these tumors against the underlying cutis or subcutaneous tissue is parallel to the surface of the skin; thus an equally thick layer of epithelium resembling the epithelial part of normal skin is formed. The clinically more malignant squamous cell carcinoma may resemble closely certain structures of the stratum spinosum, but it never forms as regular layers as many basal cell carcinomas do. This reasoning might seem helpful to some in reconciling the seemingly diverging clinical and histologic characters in basal cell carcinoma. Adami (page 799) calls the basal cell carcinoma the most aberrant and anaplastic type, and he expresses astonishment at the absence of distant metastases. He calls it "a notorious example in actual contradiction to the general rule that the extent of anaplasia is the index of malignancy." Krompecher himself calls basal cell carcinoma undifferentiated.

The rare cases of distant metastasis from an apparently benign primary tumor (myoma, goiter, chondroma) are too exceptional, and I shall not discuss them at length here; but they must be mentioned as a warning signal against overrating our knowledge about the histologic signs of clinical malignancy.

Borst recognizes that "to a certain degree" a tumor is more malignant the less mature its tissues are. He mentions carcinomas of the stomach and intestine which are slightly anaplastic but metastasize widely. Besides the well-known rare examples of disastrous malignant disease without corresponding microscopic observations, other unusual cases occur which are impressive. Hansemann (page 75 and fig. 80) gives a picture of an adenomatous tumor of the rectum "which imitates its matrix with astonishing exactitude." The patient died from recurrence. A tumor of the kidney which metastasized through many organs showed in all metastases and in the primary tumor the typical picture of benign tubular and papillary adenoma. The epithelial cells were arranged in single layers; there was no anaplasia; the mitotic figures were few (Battaglia, from Picks laboratory).

Henke, in his practical guide to tumor diagnosis, is as careful as Borst in using anaplasia for prognosis. He opposes Petersen and Collmer who made the indication for operation on cancer of the rectum dependent on the adenomatous structure; otherwise, they claim, metastasis will always occur in spite of operation. Henke points to a

case of early brain metastasis from a definitely adenomatous tumor of the rectum. Henke's book, which was written twenty years ago, contains very little about histologic prognosis.

A little more about prognosis can be found in Hertzler's treatise on tumors.

The classification of carcinoma according to the amount of connective tissue or according to the type of degeneration present is of value in certain situations in determining the prognosis. . . . The very cellular carcinomas vary in significance. They may be formed largely of cells and yet be of slow growth; but on the other hand they may be very malignant. It is the type of cell and not the number that indicates the rate of growth. . . . Usually the degree of malignancy is indicated by the alteration in the cell type.

In accordance with the arrangement of Hertzler's book, which is based on localization, there is more discussion of histologic prognosis in certain neoplastic diseases than in tumors generally. In my opinion, this way is more promising.

If the introductory general chapters in good medical books were given due attention by physicians, it would hardly be necessary in a review like this to deal with anything but the more recent literature. Unfortunately, those chapters are read too little, and so I shall quote the most important passages from Ewing's book as far as histologic prognosis is concerned. After having stated that "fortunately a parallel exists to a very marked degree between the histological structure and the usual clinical course," Ewing continues that "usually the interpretation of structure is greatly influenced by clinical information." "Pathologists and surgeons alike commonly ignore these essential conditions of accurate diagnosis, a delinquency which is responsible for the wide and firm differences of opinion regarding the relation of microscopic structure and prognosis." Ewing endorses Hensemann's view that:

The morphological evidences of anaplasia have a physiological significance in indicating the degree to which the process is freed from growth restraints and the control of organization. . . . The histologic signs of anaplasia are: a cellular character, marked variations in size, increase of chromatic nuclear substance, abundance and abnormality of mitoses, loss of polarity and diffuse infiltrative growth of cells. In many instances lack of reaction of the tissues against the infiltration of the tumor cells is a significant feature. . . . Equally important are the general signs of exalted nutrition and vitality of the cells. Upon these features one may safely base the estimate of growth capacity and potential malignancy of tumors (page 64).

In my opinion, the introduction of this term "potential malignancy" is the pivotal point of our problem. Ewing continues:

The clinical course does not always accord with the signs of growth capacity. Many factors influence the progress of growth. One must distinguish between the potential malignancy and the clinical course of tumors.

Ewing's conclusion is:

With these important limitations it may be asserted that there is a close parallel between histologic structure and malignancy.

In a paper entitled "Prognosis in Cancer," Herly makes the general statement that a tumor is the more malignant the richer it is in cells, and that those rich in connective tissue are less malignant. This may be true in many cases, but it is contradicted in many others, not only in rare tumors such as the embryonal tumors of the kidney, but also in common forms in surgical pathology, as, for instance, adenocarcinoma and scirrhous of the breast; generally the scirrhous is the more malignant form in spite of its large amount of connective tissue. Age and constitution play an important rôle in Herly's paper, and he insists that in estimating the prognosis each location must be considered differently. In his opinion,

The degree of malignancy is determined by the biology of the cancer cell itself and this determines its behaviour toward the entire organism; or, in other words, the prognosis in cancer is dependent upon the manner in which the protective forces of the organism are functioning.

This deals with the cancer cell as if it were an organism by itself, an entirely foreign body to the host, and not to some extent a part of the host's organism, which it is in our opinion. The formation of the tumor is a function of the host's organism, even if it is an extremely depraved function. We cannot in our thoughts oppose the carcinoma and the host as we oppose the tubercle bacillus and the organism. The bacillus is no part of the body, it comes from outside; whereas the cancer—whatever its origin may be—is in itself a product of the body. Modifying a much used simile, we may say that the battle between cancer and organism is not fought between two armies, but that it is a mutiny.

From a similar standpoint, we regard the term "cancer's self control" (Broders). Broders says that basal cell epithelioma controls itself by producing cells similar to the normal basal cells of the skin; but the basal cell is the one which even normally possesses the greatest power of multiplication. Cancer does not control itself. It is more or less controlled by many factors, general and local; most of them are unknown to us. What we see in the tumor cells may be related in some way to the controlling factors, but we cannot recognize these factors by studying the tumor cells.

Another prognostic system, to be applied to cancer in general has been published by McCarthy. With the many other clinical and anatomic factors, he uses four histologic ones: lymphocytic infiltration,

fibrosis, hyalinization and cellular differentiation. McCarthy gives tables for carcinoma of the stomach, breast, rectum and skin. In his opinion, the value of these four factors can hardly be questioned. All authors do not agree as to the significance of lymphocytic infiltration; some even claim that the lymphocytes open a path for the cancer (Borst, in Zweifel Payr, vol. 1, p. 22). Hansemann regarded lymphocytic infiltration as an unfavorable sign.

My chief aim is to evaluate the possibilities and limitations of histologic prognosis. This will be accomplished best by discussing special instances of neoplastic disease.

The clinically malignant tumors of the thyroid are likely to discourage one when one tries to help the surgeon with a prognosis from a slide. The data given here are the result of A. Kocher's many years of experience with the large mass of material in Bern.

Negative histologic findings in a goiter mean nothing [namely, as far as clinical malignancy is concerned]. In Langhans' embryonal adenoma only one third of the cases show malignant characters histologically. . . .

Some rare cylinder cell tumors are clinically malignant; histologically no signs of malignancy are demonstrable generally, only peculiarities in the distribution of the cytoplasm. . . .

When a parenchymatous part in the struma of a patient in the cancer age is found in active proliferation, then we must consider the tumor malignant, even when no other signs of histologic malignancy can be detected. . . .

Undoubted cancerous foci have been detected in ordinary colloid goiters; they were only a few millimeters in diameter. . . .

Certain very slow growing adenocarcinomas of the thyroid metastasize early. The cells, by irruption into the blood vessels, prove to be very malignant. Even cell groups which have invaded a blood vessel can be surrounded by a capsule. . . . Squamous cell carcinoma of the thyroid early invades the trachea, but never the blood vessels; it does not metastasize. . . . Operation for bone metastasis gives relatively good results in slow growing primary tumor. When the primary tumor can be removed the prognosis is good.

Kocher has observed a number of radical cures in such cases.

Is much comment necessary? How shall one make a prognosis from a microscopic slide when clinically malignant tumors may look harmless? Even when the whole goiter is at the disposition of the pathologist, making a definite prognosis is dangerous, one cannot make serial sections of the whole material, and the small malignant focus or the areas in which blood vessels are invaded may easily escape detection. The picture of proliferation in itself is difficult to use for prognosis; exophthalmic goiter is proliferating, but it never invades any surrounding structure, much less the blood vessels.

Basing his judgment on 108 cases, Graham arrives at the conclusion "Whether an adenoma of the thyroid is benign or malignant cannot be

decided by morphological criteria . . . if blood vessels are invaded recurrence or metastasis will follow operation, otherwise not."

Quite different is the situation regarding carcinoma of the skin. There are two kinds which are fairly characteristic both clinically and histologically: the squamous cell carcinoma which is more malignant, and the basal cell carcinoma which seldom metastasizes. The fact mentioned above that the apparently more anaplastic and less differentiated tumor, namely, the basal cell cancer, is at the same time the less malignant, may be left out of consideration.

In the book which practically has created microscopic changes of the skin, however, the classification of cancer of the skin is not made according to the cell type but according to the architecture (Unna, 1894). This elaborate classification interests us here only in its application to prognosis.

The vegetating cancers are those which proliferate most luxuriously, hence most quickly invade the contiguous area and appear in the surrounding lymph nodes. Histologically this capacity expresses itself in the widespread and equal distribution of the mitotic figures in the epithelium. The epithelium forms bulky masses.

Unna also points to the inert state of the little connective tissue which is left between the heavy epithelial masses; only surrounding the tumor as a whole, a dense, inflammatory zone is found. Since he looks at cancer growth and cancer growth control as a battle between the epithelium and connective tissue, he draws prognostic conclusions from such histologic observations.

In another form of cancer of the skin Unna finds the mitotic figures only in the lower epithelial layers, and he adds: "There is nothing of the unlimited growth which characterizes the cancers of the other group" (page 673). Styloid cancer is the name given by Unna to another type. Here the epithelial pegs taper toward the end. He explains that as a result of an energetic resistance of the connective tissue and thus as an expression of relative benignancy of the new growth. This transformation is characteristic of rodent ulcer. "Wherever the styloid tapering appears, it is a sign that at this point the new growth has stopped temporarily and that the connective tissue has successfully resisted it." About still another form of skin cancer, Unna says that it can result only from intense proliferation of epithelium and that it is correctly considered quite malignant (page 687). He finds markedly inflamed stroma, especially in the most innocent, slowly progressing forms like rodent ulcer and Paget's disease, but there are no fixed laws. He makes the important differentiation between inflammatory reactions which apparently are due to degenerative changes in the tumor epithelium,

such as hyalinization or cornification, and the inflammatory processes in the stroma which are considered as a defense against the tumor growth.

Apparently, these comments and others are not made with the intention of teaching histologic prognosis; they are rather a theoretical explanation. Nothing probably is farther away from Unna's idea than the establishing of laws for prognosis in dermatologic pathology. After reading his descriptions, however, one might be led to expect to find prognostic clues in the histologic picture, but Bloodgood's skepticism concerning cancer of the lip makes one doubtful. In a recent monograph on cancer of the skin, written by a pupil of Unna and one of his sons, an intermediate position is assumed between cytologic and architectural classification. Histologic prognosis is not referred to directly.

The same is true of Hazen's book on cancer of the skin. He makes a sharp distinction between squamous cell cancer and basal cell cancer anatomically and clinically. He emphasizes possible variations in cell form due to pressure following which prickle cells may look like spindle cells; he mentions the variations in the microscopic picture of different parts in the same tumor and of excisions taken at different times. He says further that histologically identical tumors behave differently in different localizations on the skin. The cellular infiltration, in Hazen's opinion, is generally directly in ratio with the rapidity of infiltration by the neoplasm. One may conclude from all this that Hazen is rather careful in applying histologic prognosis.

The animated discussion which practically never has stopped since Krompecher used the term "basal cell carcinoma" has some bearing on our problem. The occurrence of mixed cancers is considered more or less rare by different authors, 5 per cent by Delbanco and Unna, 15 per cent by Darier. We are more in favor of Darier's figure. Darier calls the spinocellular carcinoma the most redoubtable form and basal cell carcinoma less immediately serious. He does, not, however, make a histologic prognosis: "Le pronostic dépend essentiellement du type anatomoclinique." He, as well as Kaufmann, mentions involvement of regional lymph nodes by basal cell cancer.

In the large anatomically and clinically variegated group of basal cell carcinoma one could perhaps expect some parallelism between well-known clinical pictures and histologic observations; for these tumors grow slowly, and their different stages, even relatively early ones, can be observed clinically and histologically more easily than is possible in most other tumors. As far as we can see from the literature, however, there is no histologic criterion for the so-called carcinoma terebrans, which rather quickly invades underlying tissues, destroying them recklessly. This may be the place also to mention that Frieboes does not consider the basal cell carcinoma a malignant tumor. He writes:

"These basal cell epitheliomas³ generally have no tendency toward malignant change." He even claims that some of them are cured spontaneously.

I leave here the comparison of spinocellular and basocellular carcinoma, but I shall come back to it in discussing the histologic picture and radiosensitivity.

Broders has endeavored to make histologic prognosis for the group of the squamous cell carcinoma of the skin by a new method. It is no longer a question of making the prognosis in squamous cell carcinoma by comparing it with other tumors, but to give a prognosis in the individual case—a desirable goal. Since Broders wrote the first paper of his series on carcinoma of the lip, it seems opportune to discuss this paper here. The method has met with the approval of many surgeons throughout the country (Judd, Dieterich, Duncan and Ward, etc.). It has already influenced surgical practice, and therefore we must deal with it in a more detailed manner. Broders' basic idea is that the more highly differentiated the cells are, the lower is the malignancy of the tumor. He speaks about a grade 1 tumor when three fourths of the tumor cells or more are fully differentiated, about grade 2 when one half and grade 3 when one fourth of them are real prickly cells. In grade 4 none of them has reached this degree of maturity. Broders states that "the most important factor in squamous cell epithelioma of the lip seems to be the degree of cellular activity. The cells of some epitheliomas of the lip show a marked tendency to differentiate, that is, to produce a growth similar to normal growth; the pearly body is an example."

Cellular activity in this connection means functional activity, not growth activity, and an antagonism between cell function and cell multiplication is well known. But the question is whether the transformation into a scaly, dead, horny mass should be considered a sign

3. Freboes calls those tumors, which he considers nonmalignant, epitheliomas. For the American and for most of the English and French readers this is confusing, since they are accustomed to call the malignant squamous cell carcinoma epithelioma. In my opinion, it would be best to drop the name epithelioma from the nomenclature of malignant tumors, because different authors mean different conditions when they use the word. The word carcinoma, with or without a specifying adjective, will supplant the word epithelioma without being missed (see also Kaufmann, page 1699). The name epithelioma correctly applied means only a tumor chiefly consisting of epithelium, as for example, benign epithelioma of the skin or epithelioma adenoides cysticum, or even epithelioma contagiosum which is no tumor at all. But it is against customary nomenclature to indicate the malignant character of a tumor by a name which is derived from the histologic unit. There are special names for the malignant tumors: carcinoma and sarcoma. The historic rights of the name epithelioma in my opinion are not sufficient to warrant its further survival.

of functional activity. Would not the reverse also be true? The intercellular bridges also, by which the prickle cells are connected, are not necessarily to be explained as an organ of high biochemical function, but rather as a mechanical device. Thus we cannot recognize the prickle cell as an undoubtedly highly active one in function. We certainly agree, that morphologically it is a highly differentiated cell (pages 6 and 7).

Most readers of medical and surgical journals cannot be expected to analyze systematically the statistics which are published. Realizing the importance of Broders' papers, we have felt it our duty to make such an analysis. There is no need to bring before the reader those figures which speak in favor of the grading, but it seems to us that some of the figures given in the papers could be considered from a different point of view.

A majority of Broders' cases (62 per cent) belong to group 2. Of the cases with good results after primary operation, 67 per cent belong to group 2 and of the cases without metastasis in which operation was performed, 72 per cent (tables 11 and 14). This difference in the distribution of all cases and of the favorable cases we cannot consider striking. Table 12 refers to ten cases only, but they are of great interest; good end-results were obtained in these cases after operation in spite of metastasis. Such cases could be expected not to belong to a very malignant type, but they are equally distributed among grades 2 and 3. Since 62 per cent of all cases belong to group 2, this seemingly equal distribution means a preponderance of the prognostically bad group 3 in such unusually favorable cases.

The average duration of the lesion on the lip (table 6) for group 1 is 1.4 years, for group 2 it is 2.8 years and for group 3 it is 3.3 years. The average diameters are 1.2 cm. for group 1, 2.3 cm. for group 2 and 3.3 cm. for group 3. Thus the lesions in group 1 were relatively early and small, those in group 2 older and larger, and the lesions belonging to group 3 were still more advanced in age and size at the time when treatment was started. Hence it is not astonishing that the cases in group 1 give the best end-results and those in group 3 poorer ones. The prognosis for a patient with a small and early carcinoma is generally better than for one with a larger and older one. In the same way, it can be partly explained that cancers of the lip belonging to group 1 do not metastasize (tables 12 and 15). Do these cases run a favorable course because they are composed of a certain kind of cells, namely, the well differentiated prickle cell? The fact that carcinoma often becomes more anaplastic in the course of the disease, also increases the relative number of earlier lesions in group 1 to the seeming disadvantage of other groups. What Broders says is true for cancer of the lip, as it is for most types of carcinoma: "Some epitheliomas of the lip from the start show little or no tendency to differentiate; some grow

more malignant with time, and others increase in malignancy and then retrogress." These different possibilities of development involve another difficulty in histologic prognosis; how shall one recognize the trend of a tumor toward one of these types? To a large extent—as we have seen from Broders' tables—the microscopic picture which is supposed to warrant a favorable outcome is found coincident with other favorable factors, such as smallness of the tumor and short duration. But the value of grading and of making a prognosis from the cell type could be definitely established only by demonstrating that cases run a favorable course in spite of longer duration, larger size, youth of the patient or any other unfavorable factor, if the tumors are chiefly made up of highly differentiated squamous cells. In my opinion, this has not been proved.

In group 4, histologic prognosis is valid if one identifies this group of Broders with the class of tumors designated by others as pleomorphic or very irregular. Such very irregular microscopic pictures generally are a bad omen.

Shortly after the publication of this work on cancer of the lip, Broders wrote a similar article on cancer of the skin. Here again most of the 256 cases are classified as grade 2 (69 per cent); 17 per cent as grade 3 and 5 per cent as grade 4, while 8 per cent are classified in the favorable group 1. For cases in groups 2 and 3, that is for the majority of cases, the cures after primary operation are distributed correspondingly, 75 per cent in group 2 and 13 per cent in group 3; for group 1 also there is no striking figure, namely, 11 per cent of cures; there is no cure in group 4. The average duration of life for forty-nine patients operated on without removal of lymph nodes or salivary glands (table 18) is equal for grades 2 and 3, but much shorter for grade 1; it should be longer. In a recent paper Broders announces a slight change in grading which will shift some cases of grade 3 into grade 4. Experience will show whether this change will or will not increase the instances of reliable histologic prognosis. The method has been applied by Broders also to internal cancers of the head and neck.

Bloodgood's statements are much different. He refers, for example, to a fourteen years' cure by simple V shaped excision: "There was nothing in the gross appearance, the clinical history or microscopic pathology to distinguish this cured case from other cases in which the patient returned later with metastatic glands" (page 405). "I have been unable from a most critical investigation to find any evidence from clinical appearance or microscopic examination of the lesion in the lip which would allow one to conclude whether there is a greater or less probability of metastasis" (page 406). Several times (for example, pages 414 and 417) Bloodgood stresses the impossibility of elucidating

the factors which lead to involvement of the lymph nodes. Bartkiewicz finds that in clinically highly malignant cancers of the lip there is little inflammatory infiltration.

In a paper on the grading of carcinomas in the genito-urinary tract. Broders says that "a neoplasm can accomplish only what its cells can accomplish." That is true, but, on the other hand, a neoplasm can accomplish only what the body of the patient allows it to accomplish. Tumor growth is a function (mathematically speaking) of the behavior of the tumor and the behavior of the body. Only when we try to account for the two chief variables can we hope to make any prediction about the function. In the paper mentioned the tumors of the cervix, vagina, labium and penis are graded like skin tumors. There is an impressing difference between the figures for the cancers in the genito-urinary tract and cancers of the lip and skin; namely, a high percentage (44 per cent) of cases in grade 3, nearly equal percentages in grades 2 and 4, and only 5 per cent in grade 1. In cancer of the skin or lip more than one half of the cases belonged to grade 2 and only a few to the ominous grade 4. Further, the average sizes of the tumors are much larger than in those of the lip or skin. These tumors develop in much more hidden places than cancer on the lip; therefore they are not noticed early and they are already large when examined; here we again face the parallelism between size and duration on one hand and the less differentiated cell type on the other. Fifty-six cases of carcinoma of the bladder in Broders' article show this relation distinctly (page 589): Five tumors are small, and one of them only belongs to class 3 or 4; thirty are medium sized and two thirds of them are of grade 3 or 4; finally, of the twenty-one lesions which are large, three-fourths belong to grades 3 or 4. But this parallelism does not appear in fifteen cases of cancer of the labium; here the small lesions are equally distributed among grades 2 and 3. Of the medium sized tumors, 82 per cent belonged to grade 2; nine of these eleven patients died.

The difficulties we encountered in discussing cancer of the skin again confront us when dealing with carcinoma of the uterine cervix. Following Broders' publication, Martzloff has established a grading system for cervical carcinoma; but he includes all carcinomas in this location, not only those consisting of squamous cells. The adenocarcinoma forms one of his groups; the three others are: the spinal cell carcinoma, the transitional cell carcinoma and the fat spindle cell carcinoma. Thus Martzloff's groups cannot be compared directly with Broders' groups. The term "basal cell carcinoma" is not used in Martzloff's paper; the cells of these cervical tumors are classified by him partly as transitional and partly as fat spindle cells. Martzloff's conclusion is that the spinal cell tumor is the least malignant form in the cervix, the fat spindle cell

tumor the most malignant, while the adenocarcinoma and the tumors composed of transitional cells occupy an intermediate position. We have applied Martzloff's method to the material at the Woman's Hospital, but with the exception of an increased rate of survivals in cases with intense cornification, we could find no relation between the type of cell and the outcome of the disease. Many tumors with transitional cells were running a more favorable course than spinal cell carcinomas. Rather distinct was a group of tumors with irregular pleomorphic pictures and rapidly fatal outcome. They somewhat correspond to Broders' grade 4, but they cannot be put into any of Martzloff's groups. Most of them even were composed of spinal cells, which are considered the least dangerous cell type, and they did not belong to the fat spindle cell group. No tumors in our whole material could be classified as fat spindle cell cancers; and those which showed a large admixture of spindle cells were not more malignant than the average. In my opinion, the cell forms in cervical carcinoma do not permit of the establishing of a few groups. They are too manifold. It will be difficult to make pathologists agree on the borderlines of the cell types. The illustrations as given in several papers cannot overcome this difficulty. A close and detailed study of Martzloff's tables and of our own material has convinced us that the clinical symptoms are a better guide to prognosis today than the grouping according to cell type.⁴ There is additional difficulty in secondary changes of the tumor cells, such as flattening by pressure edematous swelling, infiltration with fat or glycogen. Such an incidental change may entirely alter the aspect of a cell without producing a corresponding change in its capacity for growth.

Many different opinions have been brought forward about the histologic picture and the prognosis in cervical cancer. Cullen and Lubarsch attribute special infiltrative power to the tumors which are composed of small cells. Ewing (page 540) states that many efforts have been made to establish a relation between prognosis and the structure of the tumor, from which it appears that the transitional cell carcinomas are distinctly more malignant than the squamous cell epitheliomas of the portio. This seems to be a comparison not only of histologic structures, but also of tumors arising in the cervical canal and of tumors originating on the portio. Whether Ewing designates as transitional the same cell elements to which Martzloff applies this term, is a question that I am unable to answer satisfactorily.

The conclusion of Schottlaender and Kermauner, drawn from their extensive study, is that "the results give little encouragement so far as a prognosis from the examination of curettings or excisions is concerned."

4. For further details, see Plaut, Alfred: *Surg. Gynec. Obst.* **93**:450 (Oct.) 1926.

Their classification includes three groups: "ripe," "middle ripe" and "unripe"; but this classification is not based chiefly on cytologic characteristics.

Oskar Frankl does not give a personal opinion on histologic prognosis. He quotes H. Albrecht who denies any parallelism between maturity of cells and rate of invasion. In a later paper, Frankl and Kraul attribute the slower course which uterine carcinoma often takes in old people to the frequency of more mature tumors in old age. This apparently involves an opinion that more mature cancers are less malignant, but it does not mean that a prognosis can be made from excised material. The question remains as to what the relation is between old age and the maturity of a tumor; the lowered malignancy does not necessarily depend on the maturity of the tumor, it might have the same cause as the maturity. Probably both are closely connected with the constitutional factor of old age; thus they would be coordinated factors. Frankl and Kraul complain that different authors follow such widely divergent principles in judging the degree of maturity in uterine cancer. They give a detailed description of their own three groups without expecting to have them generally accepted.

Mahle grades uterine carcinoma according to Broders' principles. He also finds a parallelism between the grade and the invasion in a given time. Martzloff has found that tumors of different grade invade with equal speed.

Norris and Vogt in general agree with Mahle's statement. They dwell especially on the bad prognosis of tumors with very irregular microscopic pictures.

L'Espérance for prognosis relies chiefly on the gross appearance and the location. She speaks about the rapid development of the "epidermoid carcinoma of acanthoma structure with pearl formation," thus directly contradicting Broders and Martzloff.

HISTOLOGIC PICTURE AND RADIOSENSITIVITY IN CANCER OF THE CERVIX

In the discussion of uterine cancer and of cancer of the skin, so far I have not paid attention to the radiologist's standpoint. The introduction of radiation therapy has considerably enhanced the complexity of the concept of malignancy. In spite of many exceptions and many opposing statements, the law of Bergonié and Tribondeau is widely accepted. Highly differentiated cells are more radioresistant than less differentiated ones. Clinically, greater radioresistance means greater malignancy. One is confused by finding this sign of bad prognosis in cornified squamous cell carcinoma, which is generally believed to be of a milder character (in the cervix). Susceptibility to radiation and radioresistance are complex factors about which an agreement is

not easily reached. One tumor may disappear rapidly under irradiation, but recur; another one may yield only slowly, perhaps to a heavy dose only, but without recurrence. Which of them is the more radioresistant, which the more malignant? Different answers to this question partly form the basis of the disagreement between Seitz and Wintz and Opitz. The radiologist needs, as Lahm puts it, not only a formal diagnosis giving the morphologic features, but also a functional diagnosis; one wants "information as to the growth tendency of the cancer and the defensive power of the surrounding connective tissue" (see also Caudière).

Boehm and Zweifel are among the authors who do not recognize the law of Bergonié and Tribondeau (see also Adler, O. Frankl, Kehrler, Lahm, Opitz). They see the pivotal point in the struggle between the carcinoma and the connective tissue. Hence for prognostic purposes they attempt an analysis of the relation between epithelium and mesenchyme. They consider the character of the connective tissue as important as the character of the tumor cells: "Connective tissue in which there is inflammation proliferates, connective tissue which is at rest, does not" (page 32). The emphasis of Boehm and Zweifel's classification is placed, not on the form of cell, but on the form of the epithelial masses and on the inflammatory reaction in the stroma. This reminds one of Unna's classification of cancer of the skin, which, however, was not undertaken with a special view concerning prognosis based on the microscopic picture, as Boehm and Zweifel's classification is. Their most important observation is "When the epithelium of the portio invades the connective tissue in the form of thick pegs, then the prognosis for radiotherapy is poor. But when we find small islands of epithelium surrounded by young connective tissue, the prognosis is favorable." Next to this mass and surface relation between epithelium and stroma, they consider the behavior of the connective tissue, the degree and character of cellular infiltration, the maturity of the tumor cells, the relation between nucleus and plasma and the degree of leukocytic infiltration in the tumor itself. The mitotic figures to them have no bearing on prognosis. Of one hundred and twenty-two cases which could be used for comparison, their prognosis was correct in ninety-two and in thirty it failed; among these thirty were ten cures in spite of bad prognosis made from the microscopic slide examination. It is most interesting to read the description Boehm and Zweifel give of the tumors most suitable for irradiation and of these least suitable, while keeping in mind other prognostic systems, as, for instance, those of Martzloff and Broders. "Best suited for irradiation are: the carcinoma medullare with immature cells having much highly vacuolized plasma, with intense leukocytic infiltration in the epithelium and stroma, with young granula-

tion tissue. Most unfavorable is the highly differentiated cancer with a tendency toward cornification, large epithelial plugs and connective tissue without leukocytic infiltration. The leukocytes in the area about the cornification cannot be considered a favorable sign. All patients with such cases, irrespective of the class they belonged to, died. Cornification alone, when other conditions are favorable, does not prevent cure." Direct contradiction to Martzloff's conclusions is evident. Boehm and Zweifel believe that cervical carcinoma may be classified in the future into two kinds: cervical carcinoma accompanied by leukocytic infiltration in the stroma and the type in which such an infiltration is absent. Two years ago, when I tried to establish a relation between the histologic picture and prognosis, I paid special attention to the thickness or thinness of the epithelial strands and pegs and to the character of the connective tissue, also to the intensity, distribution and character of the inflammatory reaction. The results were negative. In order to illustrate the place in clinical work which Boehm and Zweifel attribute to their prognostic method, I shall quote two sentences from their paper: "These results justify us in considering this histologic analysis as of practical value. Using it with reservation we shall be able to give a relatively certain prognosis concerning the results of radiation." But the last paragraph of the paper reads: "In the majority of cases naturally conditions are not entirely favorable or unfavorable. In such cases judgment and prognosis are much more difficult, and so far uncertain."

Boehm and Zweifel ask whether in these histologically intermediate groups one could not perhaps first try to create more favorable histologic conditions and then use radiation. This is the worst part of the problem. None of the many authors has made clear his view on the causal relation between histologic structure and clinical course. Do the observers avoid the more or less subconscious belief that certain histologic features are responsible for a certain course of the disease? Another point of view regards them only as a sign, a symbol of certain biologic processes. Inflammation in the stroma might indicate a certain resistance of the connective tissue; but when we start any inflammation in the connective tissue artificially, do we convey to the stroma an identical or even similar power of resistance? Part of Boehm's and Zweifel's material was examined by Schoch to determine the character of the inflammation. In 10 per cent he found marked local eosinophilia; these cases gave good results with irradiation.

The most original method of histologic prognosis is that tried by Lahm. An accurately standardized radium tube is put on the tumor for a few hours, and from the same spot a biopsy is taken four days later. This is Lahm's functional diagnosis. The character and intensity of the changes in the tumor cells are not given much consideration; the inflammatory reaction is the important thing. Eosinophils in large number indi-

cate a good prognosis; plasma cells and polymorphonuclear leukocytes indicate a lack of reaction of the body. Lahm's figures are impressive: In thirty-six cases of reactive eosinophilia fourteen patients were cured and nineteen died; three could not be traced. In one hundred and twenty cases without reactive eosinophilia twenty-one patients were cured and eighty-nine died; one was not traced. The important thing is not the presence of eosinophils in the tumor before treatment, but their appearance during and after irradiation. The eosinophilia is rather conspicuous in progressing and advanced carcinoma. In spite of his figures, Lahm speaks only about "orientation concerning the possibility of primary or secondary cure at least to a certain degree."

Henry Schmitz, in two papers, places in juxtaposition the two statements that basal cell carcinoma of the cervix is more malignant because the basal cell is less differentiated and that squamous cell carcinoma and adenocarcinoma require a much higher dosage of radiation.

Pomeroy and Strauss obtained their best results with irradiation in the group of squamous cell carcinoma with cornification. They attribute their good palliative results in the transitional cell type to the susceptibility of the transitional cell, and explain it by low differentiation. In the tumors composed of broad spindle cells—certainly a still less differentiated type—they were less successful in giving relief.

In the opinion of Bowing, the grading of a biopsy specimen is necessary in order to prevent hemorrhage or secondary infection after irradiation.

Summing up the matter of histologic prognosis in cervical carcinoma, I may say that there is a bewildering mass of contradictions and misunderstandings in a matter of greatest practical and theoretical importance.

A few remarks may be inserted here about radiosensitivity and malignancy in cancer of the skin and other organs. Lachapède claims that the primary results of irradiation in cancer of the skin do not depend on the histologic structure; they are the same for squamous cell carcinoma and basal cell carcinoma. He relies entirely on the number of mitoses; the figures he gives are not convincing. Lacassagne is of the same opinion.

Rost says that there is some possibility of determining the degree of radiosensitivity from the microscopic picture. The largest number of refractory cases is found among patients with squamous cell cancers. Regaud has been able "for many years by the selective radiation treatment to obtain a greater proportion of cures in squamous cell carcinoma than in basal cell carcinoma. The idea of the radioresistance of the spinocellular tumors and of the difficulty of curing patients who have them must be changed." Darier, however, calls the squamous cell carcinoma very radioresistant.

At the cancer congress in 1923, the discussion on radiosensitivity, histologic structure and prognosis showed the same wide divergence of opinions as can be found in the American and German reports. Some of the authors tried to use a karyokinetic index for determining the sensibility; others considered the behavior of the stroma the most important factor. Some even expressed the idea that one should not use irradiation for a tumor (of the breast, for instance) without knowledge about its stroma, because there is danger of killing an active stroma.

In the various forms of basal cell carcinoma of the skin differences in radioresistance exist. Hazen reports less than 3 per cent of failures in the common rolled edge type, whereas it is 17 per cent in the ulcerative type and 55 per cent in the deep nodular type. All these tumors are composed of the same kind of cells, but they differ in external gross features and in microscopic architecture. According to Hazen, basal cell carcinomas in different locations react differently to irradiation. In two failures in basal cell cancer of the ear there was no inflammatory infiltration surrounding the carcinomatous tissue in the cartilage. Similar observations were made on cancer nodules in the area about a surgical scar and in the center of a roentgen-ray scar; but in another case of failure Hazen found a marked inflammatory reaction together with endarteritis. Nevertheless, there was no evidence of death in any of the cancer cells. In these instances also a histologic explanation of the resistance cannot be given. And why do basal cell cancers which are situated near the lip often react poorly to irradiation?

A new complication appears in a short statement which Regaud makes about cancer of the cheek. The primary lesion in the epidermoid carcinoma, he says, is favorable to radium therapy but the adenopathies arising are of an unfavorable histologic nature, especially for roentgenotherapy. Squamous cell tumors are not unfavorable in Regaud's opinion; it would be interesting to learn what histologic picture or what other factor in these regional metastases is considered the source of this unfavorable behavior. Quick saw rapid progress of the disease in carcinoma of the buccal mucosa.

A special paragraph on histologic structure and prognosis is found in Lockwood's monograph on cancer of the breast; but its object is only to show that a prognosis based on the histologic picture cannot be made.

In 1922, Ewing (page 508) stated that anatomic structure and histogenesis of breast cancer are not enough understood for any significant knowledge on etiology, prognosis and value of treatment. His classification relies partly on the gross appearance, partly on the microscopic structure. The age and condition of the patient and the condition of the breast in which the tumor originates are considered most important

as influencing the course of the disease. Outspoken adenomatous structure is regarded as a favorable sign; the rare, highly malignant, soft "encephaloid" adenocarcinomas are mentioned especially. Possible differences in the histologic structure of the primary tumor and the axillary metastases are emphasized. For certain cancers of the breast, Ewing establishes three grades of malignancy according to form and arrangement of the cells. There are no uniform histologic observations in acute carcinosis of the breast. Lee and Tannenbaum found different histologic pictures in twenty-eight cases of acute inflammatory carcinoma of the breast.

A system of prognosis has been established by Greenough in which the chief histologic character considered is that of the adenomatous structure. Originally his classification included four groups: a group in which there was a definite differentiation, one with moderate differentiation, one with slight differentiation, and a group containing the highly malignant forms. Later, three groups were established: tumors of slight, medium and high malignancy (groups 1, 2 and 3). Of nineteen patients in group 1, thirteen were cured; eight had lymph node involvement, including four who were cured. Of thirty-three patients in group 2, eleven were cured; twenty-six had lymph node metastasis, including eight who were cured. In the third group, none were cured; in five cases of group 3 no lymph nodes were involved. Attention was directed especially to retention or loss of the adenomatous arrangement of tumor cells around an open space, to the evidences of secretory activity (vacuoles) in the cell protoplasm, to nuclear changes, hyperchromatism, number of mitoses, irregular mitoses and to variations in size and form of the cell and the nucleus (pleomorphism). The cures in group 1 with involvement of lymph nodes speak in favor of this classification. Greenough considers the presence of mucoid droplets a good indicator of lower malignancy; they are a sign of secretory activity and of cell differentiation. The size of cells and nuclei is in itself unimportant, but varying size indicates high malignancy (page 458). Round cell infiltration is no sign of resistance; it accompanies necrosis, which itself appears to have little to do with prognosis. Hyalinization is not a favorable sign. Greenough concludes that in cancer of the breast the degree of malignancy can be determined with reasonable accuracy by study of the histologic picture. He calls the classification important in prognosis; it should be of assistance in estimating the value of therapeutic measures. "The pathologic classification of these specimens, however, can hardly be reduced to rule of thumb, but rests upon the estimate of the individual observer and the weight he is inclined to attribute to a number of different factors." The probable general rule that histologic prognosis is best made in the

extreme forms of tumor and is more difficult in intermediate forms, applies to Greenough's grading system also, for the architectural as well as for the cytologic criteria. In the tables, the groups of high degree of hyperchromatism and mitosis contain few cases. Perhaps the importance of such marked variations could be shown for more cases if the dividing line between a moderate and a high degree of hyperchromatism were drawn at another point (the same being true for mitosis). In some respects this would correspond to the change Broders recently has made in his system.

Lee and Herendeen make a prognosis on the basis of the histologic picture only when the histologic picture is irregular and when the tumor is a relatively benign papillary cystadenocarcinoma of the breast. They generally determine the degree of malignancy by age, rate of growth, histologic appearance and axillary involvement.

Delbet and Mendaro examined the tissue of cancer of the breast for secretion granules and for mucin. From a total number of fifty patients, one-third were alive after four years; all of the thirteen in whose tumors secretion granules had been found were alive, and only one of them had a recurrence. In cases in which otherwise the advisability of operating is doubtful, the presence of secretion makes the chances of successful operation good. The authors do not base their whole prognosis on secretion, but they consider it an important factor.

In the opinion of Wyard, only the size of a tumor of the breast is important for the prognosis, not the histologic picture, not even the age.

Lane-Clayton finds a higher percentage of cures in adenocarcinoma. His statistics cover more than 1,000 cases.

It seems to me that cancer of the breast offers better opportunities for histologic prognosis than uterine cancer. Colloid cancer of the breast has found no place in Greenough's classification, perhaps on account of its relative rareness. Most authors agree as to its lower degree of malignancy (Williams, Lange, Gaabe, Kaufmann, Ewing and many others). In the early literature also this opinion is found (Lebert, Schuh, Thompson, Bryant, Klebs). Others, like Despres, Georg and B. Schmidt, claim that colloid cancer is often very malignant. Slow growth, rare and late involvement of lymph nodes, absence or regional restriction of metastases and absence of cachexia are the chief characters referred to in the descriptions of gelatinous carcinoma of the breast. Many of the colloid cancers are found in old women. In this connection we remember that the relatively benign cystic adenocarcinoma shows the same preference (Ewing, page 513) and that, according to Frankl and Kraul "riper" carcinomas of the uterus are more frequent in older women. I recently saw a gelatinous carcinoma of the breast in a woman 83 years old; eight years previously she had been operated

on for an early papillary cystadenoma in the same breast. Further experience is necessary before we can decide whether it will be helpful for histologic prognosis to divide the group of colloid cancer into two groups, for gelatinous masses may be derived from the epithelium or from the connective tissue. The absence of signet ring cells is considered by Herzog as a diagnostic sign that the colloid material does not come from the epithelium but from the stroma. He never saw signet ring cells in cancer of the breast, and he puts the gelatinous cancer of the breast near the cylindroma (Billroth); he points to their clinical resemblance, slow growth, tendency to recurrence and rarity of distant metastases.

Kaufmann does not include all cylindroma-like tumors of the breast in the group of colloid cancer. Apparently he thus refers to the gelatinous change of stroma which occasionally is found in ordinary duct cancers (Ewing, page 496). Although we are far from a complete understanding of colloid cancer of the breast and its different forms, it seems to me that this change can be used as a favorable point in prognosis—certainly only one point in combination with many other clinical and anatomic ones.

Much fewer data are available for judging the prognostic value of gelatinous change in cancer of other organs. Eugen Fraenkel with his wide experience denied that colloid cancers were less malignant than others. In the detailed chapter on cancer of the stomach recently written by Borrmann I could not find any reference to the prognosis of colloid carcinoma of the stomach. Zimmer saw more permanent cures in gelatinous carcinoma of the rectum than in other types of rectal cancer.

Colloid carcinoma grows chiefly locally by extension. Therefore in the breast it does not so quickly find vital parts to destroy, but in the alimentary canal conditions are different. This may partly explain why the relatively low malignancy of colloid cancer is more conspicuous in the breast than in the stomach and intestine where "wandering on a wide front" (Aschoff) leads to disastrous invasion of peritoneum.

This review could be arranged as is material in books on general pathology; the subject matter being divided into discussions on inflammation, edema, necrosis, hyalinization, etc., in tumors and their relation to the degree of malignancy. This would lead to many repetitions. To inflammation, for instance, a variety of prognostic meanings has been attributed which renders a general judgment of the question nearly impossible.

Information concerning the relation between local histologic factors and general constitutional ones is meager. A few have been mentioned (page 43); I do not doubt that many more exist. The difference in

attitude of pathologists on this point is shown by their desire to have clinical data accompanying the specimen or by a relative indifference to clinical data. While some (including myself) want as much clinical information as they can possibly get, others warn against the danger of being biased in judgment by clinical data (Broders).

That the occurrence of certain carcinomas is closely associated with constitutional factors, we know. Is the course of the disease affected by these factors? Are these two problems related in any way? Although I am not able to answer, I thought it worth while to bring up the question.

The problem of mitosis requires a chapter of its own. The belief prevails that the number of mitotic figures is a fair indicator of the degree of malignancy. This belief has been severely shaken. I have often wondered how one should account for a rate of growth due to amitotic cell division, which does not as a rule give such typical, easily detected pictures as mitosis does. The textbooks on histology and pathology generally hardly mention amitosis (Stoehr, Rauber-Kopsch, Schmaus, Aschoff, McCallum, Tendeloo). In monographs on tumors amitosis is seldom mentioned. Delbanco and Unna, Jr. (page 19) refer to numerous mitoses and amitoses in the highly malignant "carcinoma globocellulare" of the skin. Horst Oertel takes a different stand; in his experience, "the common method of cell division in different tissues is amitosis and not karyokinesis. Mitosis appears more frequently under difficult and complicated methods of division. Many figures and changes which have been described as mitotic in pathologic conditions are degenerative nuclear phenomena. Often the lack or scarcity of mitosis even in rapidly growing tissue is striking (division by amitosis). Mitosis is therefore not necessarily an index of cell proliferation."

If this statement could be proved, even partly, it would detract considerably from the value of counting the mitotic figures in a tumor.

Karl Peter refers to the neglect of observations on amitosis since indirect cell division with its manifold new data has become known. "Only in recent times has interest returned to direct (amitotic) cell division and its relation to the indirect (mitotic) one."

According to Palugyay, in immature carcinoma of the cervix uteri, a shortened type of cell division frequently takes place without disappearance of the nuclear membrane and without formation of a spindle, the whole process being somewhat similar to amitosis. Ewing also (1919, page 39) says that "amitosis is frequently observed in rapidly growing tumors and in some cases may be the chief mode of cell division."

It seems to me that the interesting picture of mitosis is the chief underlying cause for its high valuation and for the resulting neglect of amitosis, just as we speak more about the blood than we do

about the lymph. Cold, stimulating substances, autotoxins and increased metabolism lead to amitosis (Benninghoff). Certainly this is reason enough to consider amitosis in tumor growth seriously. In my opinion, much work is needed before we shall know enough about the relative importance of both kinds of cell division and before we shall be able to consider their occurrence in making a prognosis. Peter has demonstrated experimentally that the epithelial cells in the kidney tubules of larvae of salamandra do not contain vacuoles during mitosis. That means absence of resorption; but the presence of granules shows that another function continues during mitosis, namely, the chemical transformation of the resorbed material. In the cells of the stomach and pancreas which are in mitosis secretion granules are absent six hours after feeding, when all the surrounding cells are full of them; but the expulsion of the already secreted material into the lumen goes on during mitosis. We know that some cells during mitosis lose their filamentous or ciliary structures, thus showing transitory loss of special functions. It can also be demonstrated that the growth of cells stops during indirect division. Peter has succeeded in preventing mitosis by stimulating function. He injected pilocarpine into the larvae of salamandra and then counted the number of mitotic figures in the renal tubules; the result was a striking diminution of mitoses in the injected animals, the kidneys of which were stimulated to increased function by the pilocarpine. Thus we have an experimental basis for an antagonism between mitosis and function. Mitosis could be taken as an indicator for the loss of functional differentiation. Amitosis, however, does not interfere so much with function and perhaps is not inhibited in such a marked degree by increased function. On the other hand, functional stimulation also leads to growth, and the question of formative stimuli independent of decrease or increase of function still is unanswered. Peter asks whether malignant growth continues when a tumor shows secretory activity; it can do so, as Eiselsberg's famous case proves. Thyroidectomy was performed on his patient for a malignant tumor; he developed myxedema; a distant metastasis appeared, and the myxedema subsided. After removal of the metastasis, however, the patient became myxedematous again. Evidently malignant liver tumors as well as their bone metastases can produce bile (Kaufmann, page 754). These are exceptions, but it will be good to bear them in mind when signs of secretory activity in a tumor tempt one to make a more favorable prognosis.

Since Hansemann the number of mitotic figures and the presence and number of atypical mitoses are the two things to which attention is generally paid. As mentioned above, Unna considers their distribution also. He takes it as a sign of rapid growth when the mitoses are

widely and equally distributed through the whole thickness of the cell strands in a squamous cell cancer. In skin tumors of slower propagation Unna finds the mitoses chiefly located near the basal layer. We consider this old observation important. Regaud directs his therapeutic efforts in skin carcinoma only against the mother cells which occupy the periphery of the cell cords or lobules of the tumor tissue, the generating cells. He declares that all the other cells belong to lateral branches, the end product of which is the sterile, horny squamous cell. We must admit that we do not understand why the multiplication of squamous cells in cancer should be limited, when we see so many mitoses far away from the basal layer. If radiation attacks cells it would be well perhaps to account for these upper layers also.

The only detailed study of mitosis in a special neoplastic disease and with respect to the clinical facts is that of Palugyay. With very careful technic, Palugyay has analyzed the slides of many cervical cancers and has selected 147 cases which were suitable for his investigation. He has found a certain parallelism between the maturity of the tumor and the number of mitotic figures, but no simple numerical relation to mitosis as a whole. One must regard the different phases of mitosis separately. In immature cancers of the cervix many prophase are found and few true mitotic figures of the later phases (metaphasis and anaphasis). In maturing and advanced cancers less prophase are seen and more typical mitotic figures. Palugyay's explanation is that in immature tumors many nuclei enter the first phase of indirect division, the prophase, but then a kind of shortened division takes place, and no typical mitotic figure (metaphasis, anaphasis) is formed. This process, intermediate between mitosis and amitosis, has been named indirect nuclear fragmentation by Borst. Knotty and asymmetrical mitoses are especially frequent in immature cancers. Multipolar and very large mitoses are frequent in more mature tumors. Other atypical features of mitosis are found in cancers of different degrees of maturity. So far I have quoted Palugyay's data.

The conclusions are obvious. It would be misleading to judge the degree of malignancy from the number of mitotic figures. It would be misleading to use the striking multipolar mitoses and the giant mitoses for a more unfavorable prognosis. While reading Palugyay's paper I remembered that often in cervical carcinoma I had seen the prophase without being sure how to interpret them; I also frequently see typical metaphases in well developed large prickly cells. A similar careful analysis of the cell division in other tumors would probably repay one.

Summing up the discussion on mitosis and other forms of cell division, we are sorry to state that here too we face more problems than we possess facts which could be used for histologic prognosis.

COMMENT

The present possibilities of histologic prognosis are smaller than would appear from the examples given. Conclusions have been drawn from follow-up investigations, but in only a small number of these cases has it been possible to make a histologic prognosis from an excised tumor fragment. Histologic prognosis can be safe only when the tumor is homogenous and when it runs true to course, that means when it does not change its structural and biologic character during the progress of the disease. Carcinoma of the cervix, for instance, fulfils neither of these conditions in a sufficient degree.

General histologic prognosis is feasible in rare instances only; more promising are the endeavors to establish histologic prognosis for special tumors in special locations. The method of clinical statistics is subject to great errors, and only very large figures from homogenous material which are obtained by the same method throughout, can be made the basis for positive conclusions. The many contradictory statements quoted above show that only too well. After extensive studies in such special histologic prognosis, it may be possible in the future to determine which rules for general prognosis will remain; perhaps it will be only those governing the bad prognosis to be made from the highly irregular, pleomorphic structures.

The interpretation of the most used histologic features is so far uncertain. This is true of inflammation in the stroma and in the epithelium itself, maturity of cells and anaplasia and also of the mass relation between epithelium and mesenchyme.

Knowledge of cell division in tumors requires much more study with special reference to the occurrence of amitosis, of intermediate forms of cell divisions and of the different phases of true mitosis. The distribution of the cell divisions may be important also. In order to discuss the term "malignancy," it is necessary to consider separately local extension, metastasis, recurrence, cachexia, local regression during irradiation and occurrence of metastasis after irradiation. Constitutional factors, such as age, race and sex, must be studied in their interrelations with microscopic pictures.

Histologic prognosis can be a great help to the physician if he is always aware of its limitations. There may be disappointment sooner or later when prognoses are made from microscopic slide examination according to standardized rules. Only the most careful study of individual cases can avail us in the presence of the manifold histologic and clinical phases of malignant tumors.

[NOTE.—While this paper was in press another article of Broders appeared (*Carcinoma, Grading and Practical Application*, Arch. Path. 2: 376, 1926). I fully agree with Broders that it is important to

make people realize the wide differences in the degree of danger involved in diseases which are all called cancer. I do not consider the time ripe, however, to advocate the method of histologic prognosis for practical purposes. As far as the comparison between Martzloff's transitional group and Broders' grade 3 is concerned, the reader is referred to page 252 of this review and to my article in *Surgery, Gynecology and Obstetrics*. An opinion on the statistical data as given by Broders and by W. Hueper (in the discussion) could be formed only after a detailed analysis, taking into account the size of the tumors, the duration of disease, etc. (see the paragraph on cancer of lip in this review)].

BIBLIOGRAPHY

- Adami, J. G.: The Principles of Pathology, Philadelphia, Lea and Febiger, 1920.
- Albrecht, H., quoted from Frankl, O.: Pathologische Anatomie und Histologie der weiblichen Genitalorgane, Leipzig, F. C. W. Vogel, 1914.
- Adler, quoted from Boehm and Zweifel, Zentralbl. f. Gynäk. **50**:30 (Jan.) 1926.
- Von Bartkiewicz: Ueber Entstehung und Wachstumsverhaeltnisse des Unterlippenkarzinoms, Ztschr. f. Krebsforsch. **17**:120, 1919.
- Battaglia, P.: Ueber Carcinoma adenomatodes ("Adenoma destruens") der Niere, Virchows Arch. f. path. Anat. **250**:555, 1924.
- Bloodgood, J. C.: Carcinoma of the Lower Lip: Its Diagnosis and Operative Treatment, Surg. Gynec. Obst. **18**:404 (April) 1914.
- Benninghoff, quoted by Peter: Klin. Wchnschr. **3**:2177, 1925.
- Borrmann, R.: Geschwuelste des Magens und Duodenums, in Henke-Lubarsch: Handbuch der speziellen pathologischen Anatomie und Histologie, vol. 4, pt. 1, 1926.
- Borst, Max: Die Lehre von den Geschwuelsten, 1902; idem in Zweifel-Payr: Die Klinik der Bösartigen Geschwülste, Hirzel, 1925.
- Boehm and Zweifel: Inwieweit kannman heute aus mikroskopischen Befunden eine Prognose fuer die Bestrahlung des Uteruskarzinoms stellen? Centralbl. f. Gynäk. **50**:30 (Jan.) 1926.
- Bowing, H. H.: Surgery, Radium and Roentgen Rays in the Treatment of Carcinoma of the Cervix, Am. J. Obst. Gynec. **11**:400 (March) 1926.
- Broders, A. C.: Cancer's Self Control, M. J. & Record **121**:133 (Feb.) 1925; Squamous Cell Epithelioma of the Skin, Ann. Surg. **73**:141 (Feb.) 1921; Squamous Cell Carcinoma of the Lip; A Study of 537 Cases, J. A. M. A. **74**:656 (March) 1920; Grading of Carcinoma, Minnesota Med. **8**:726 (Dec.) 1925; Epitheliomas of Cavities and Internal Organs of Head and Neck, Arch. Surg. **11**:43 (July) 1925; Epithelioma of the Genito-Urinary Organs, Ann. Surg. **75**:574 (May) 1926; Some Practical Surgical Pathological Observations and Deductions, J. A. M. A. **80**:104 (Jan. 13) 1923.
- Caudière: Reciprocal Action of Epithelium and Connective Tissues in Malpighian Epithelioma: Its Relation to Cell Growth, Compt. rend. Soc. de biol. **93**:358 (July 10) 1925.
- Cullen, quoted by Ewing: Neoplastic Diseases.

- Darier, D. J.: *Précis de Dermatologie*, Paris, Masson et Cie, 1923.
- Delbanco, E., and Unna, G. W.: Die Boesartigen Geschwuelste der Haut, in Zweifel-Payr: *Die Klinik der Boesartigen Geschwuelste* **1**, 1924.
- Delbet, P., and Mendaro, A.: Prognosis in Secretory Epithelioma of Breast, *Bull. Acad. de méd. d. Paris* **93**:463 (April 28) 1925.
- Dieterich, F. H.: Grading Tumor Malignancy, *J. S. Carolina M. A.* **21**:143 (June) 1925.
- Duncan, R., and Ward, E. D.: *The Grading of Epitheliomata*, New York M. J. **118**:681 (Dec.) 1923.
- Ewing, J.: *Neoplastic Diseases*, Philadelphia, W. B. Saunders Company, 1919.
- Fraenkel, Eugen: Personal communication.
- Frankl, O.: *Pathologische Anatomie und Histologie der weiblichen Genitalorgane*, Leipzig, F. C. W. Vogel, 1914.
- Frankl, O., and Kraul, L.: Lebensalter und Reifegrad des Karzinoms, *Wien. med. Wchnschr.* **75**:1285, 1925.
- Frieboes, in Riecke, E.: *Lehrbuch der Haut und Geschlechtskrankheiten*, 1921.
- Graham, Allen: Malignant Epithelial Tumors of the Thyroid, *J. M. Research* **44**:660, 1924; Malignant Tumors of the Thyroid, with Special Reference to Invasion of Blood Vessels, *Surg. Gynec. Obst.* **39**:781 (Dec.) 1924.
- Greenough, Robert B.: Varying Degrees of Malignancy in Cancer of the Breast, *J. Cancer Research* **9**:451, 1925.
- Hansemann, David: Studien ueber die Spezifitaet, den Altruismus und die Anaplasie der Zellen, 1893; *Die Mikroskopische Diagnose der Boesartigen Geschwuelste*, Berlin, A. Hirschwald, 1902.
- Hazen, Henry H.: *Skin Cancer*, St. Louis, C. V. Mosby Company, 1916; Lessons Learned from Failures in the Roentgen Ray Treatment of Cutaneous Cancer, *J. Cancer Research* **9**:404 (Sept.) 1925.
- Henke, Friedrich: *Praktische Anleitung zur Untersuchung von Geschwuelsten*, Jena, Gustav Fischer, 1906.
- Herly, L.: Prognosis in Cancer, *M. J. & Record* **122**:509 (Nov. 4) 1925.
- Hertzler, Arthur A.: *A Treatise on Tumors*, Philadelphia, Lea & Febiger, 1912.
- Herzog, G.: Ueber den Gallertkrebs der Brustdruese, *Centralbl. f. Pathol.* **35**:4, 1925.
- Judd, E. Starr: The Surgical Treatment of Cancer, *J. A. M. A.* **84**:10 (Jan. 3) 1925.
- Kaufmann, E.: *Lehrbuch der Speziellen Pathologischen Anatomie*, 1922, vol. 2, p. 1712.
- Kehrer: *Verhandl. d. Deutsch. Gesellsch. f. Gynäk.*, 1922 and 1923.
- Kocher, Albert: Die malignen Tumoren der Schilddruese, in Zweifel-Payr: *Die Klinik der Boesartigen Geschwuelste*, 1924, vol. 1.
- Krompecher: Der Basalzellenkrebs, 1903; Ueber Gesetzmaessigkeiten im Aufbau der Krebse, *Ztschr. f. Krebsforsch.* **22**:410 (Aug.) 1925.
- Lacassagne, A.: *Paris méd.* **13**:376 (April 28) 1923.
- Lachapède: *Paris méd.* **13**:540, 1923.
- Lahm, Wilhelm: *Verhandl. d. deutsch. Gesellsch. f. Gynäk.*, 1922; *Arch. f. Gynäk.* **117**:264 (June) 1922.
- Lane-Clayton, quoted by Blackburn, J. H.: Prognosis in Cancer of Breast, *Kentucky M. J.* **24**:56 (Jan.) 1926.

- Lange, F., quoted by Wolff, J.: *Die Lehre von der Krebskrankheit*, vol. 2, p. 1120.
- Lee, Burton J., and Herendeen, Ralph E.: An Evaluation of Preoperative and Postoperative Radiation in the Treatment of Mammary Carcinoma, *Ann. Surg.* **82**:404 (Sept.) 1925.
- Lee and Tannenbaum: Inflammatory Carcinoma of Breast, *Surg. Gynec. Obst.* **39**:580 (Nov.) 1924.
- L'Espérance, Louise S.: Early Carcinoma of the Cervix, *Am. J. Obst. & Gynec.* **8**:461 (Oct.) 1924.
- Lockwood, C. B.: *Cancer of the Breast*, London, H. Frowde, 1913.
- Lubarsch, quoted by Ewing.
- McCarthy, W. C.: Prognostic Factors in Cancer, *Ann. Clin. Med.* **2**:244 (Jan.) 1924.
- Mahle: The Morphological Histology of Adenocarcinoma of the Body of the Uterus in Relation to Longevity, *Surg. Gynec. Obst.* **36**:385 (March) 1923.
- Martzloff, K. H.: Carcinoma of Cervix Uteri: Pathological and Clinical Study with Particular Reference to the Relative Malignancy of the Neoplastic Process as Indicated by the Predominant Type of Cell, *Bull. Johns Hopkins Hosp.* **34**:141 and 184 (June) 1923.
- Norris and Vogt: Carcinoma of Uterus, *Am. J. Obst. & Gynec.* **2**:550 (May) 1924.
- Oertel, Horst: *General Pathology*, New York, Paul B. Hoeber, 1921, p. 206.
- Opitz, Friedrich: On the Radiation Biology of Carcinoma, *Brit. J. Radiol.* **30**:252 (July) 1925.
- Palugyay, J.: Reifestadium des Karzinoms und Zellteilung, *Ztschr. f. Krebsforsch.* **22**:251 (April) 1925.
- Peter, Karl: Ueber Zellteilungsprobleme, *Klin. Wchnschr.* **3**:2177 (Nov. 25) 1925.
- Petersen and Collmer, quoted from Henke.
- Plaut, Alfred: The Relation of Prognosis to the Histological Findings in Carcinoma of the Cervix, *Surg. Gynec. Obst.* **93**:450 (Oct.) 1926.
- Pomeroy, Lawrence A., and Strauss, Abraham: Carcinoma of the Cervix Uteri, *J. A. M. A.* **88**:1060 (Oct. 4) 1924.
- Quick, Douglas: Radium Report of the Memorial Hospital, New York, Paul B. Hoeber, sér. 2, 1923.
- Regaud, C.: Some Biological Aspects of Radiation Therapy of Cancer, *Am. J. Roentgenol.* **12**:97 (Aug.) 1924; On Curietherapy of the Epitheliomata of the Tongue and of Their Following Adenopathy, *Brit. J. Radiol.* **30**:361, 1925.
- Schmitz, Henry: A Study of the Action of Measured Radiation Doses on Carcinomata of the Uterine Cervix, *Am. J. Roentgenol.* **10**:781 (Oct.) 1923.
- Schmitz, Henry: The Treatment of Inoperable Cervical Carcinomata with Measured Doses of X-Ray and Radium Based on Microscopic Examination. The Five Years End Results, *Am. J. Obst. & Gynec.* **9**:644 (May) 1925.
- Schoch, E. O.: Eosinophile in Probeexcisionen von Portiokarzinom. *München. med. Wchnschr.* **72**:380 (March 6) 1925.
- Schottlaender and Kermauner: *Zur Kenntnis des Uteruskarzinoms*, 1912.
- Unna, P. G.: *Die Histopathologie der Hautkrankheiten*, Berlin, A. Hirschwald, 1894.

- Virchow, Rudolf: Die Krankhaften Geschwuelste 2:268, Berlin, A. Hirschwald, 1863.
- Williams, W. R.: A Monograph on Diseases of the Breast, London, John Bale & Sons, 1894.
- Wolff, J.: Die Lehre von der Krebskrankheit, pt. 1, Jena, Gustav Fischer, 1907.
- Wyard, S.: Cancer of the Breast: An Attempt to Estimate Duration of Life After Operation, *Lancet* 1:1179 (June 6) 1925.
- Zimmer: Wiener klin. Wchnschr., 1909.

Notes and News

New Quarters at Northwestern.—The departments of bacteriology and pathology of Northwestern University Medical School in Chicago have moved into their new quarters in the Montgomery Ward Memorial Building at 303 East Chicago Avenue. The teaching laboratory for both departments consists of five units, each accommodating twenty-four men, and separated by clear glass partitions. Well equipped research laboratories have been provided for both departments. The Zeit Museum of Pathology will be adequately housed on the same floor with the department of pathology.

Teaching in Warren Museum at Harvard.—The Warren Museum of Harvard University is now an integral part of the department of pathology. Myrtelle M. Canavan is curator. Important alterations have been made adapting the museum for teaching purposes in pathology. Special tanks for the storage of unmounted gross specimens have been installed. The museum is used extensively evenings by the students of the second year for conferences and review purposes. They are given free access to the teaching collections of gross material and to about 5,000 lantern slides of pathologic conditions.

Experimental Pathology at Harvard.—A suite of four rooms has been furnished and equipped for a laboratory of experimental pathology under the supervision of Charles L. Connor, now in charge, on leave of absence of the laboratories of the Montreal General Hospital.

New Veterans Hospital at University of Oregon Medical School.—The United States Veterans Hospital no. 77, in Portland, Ore., plans the construction of new buildings on a site of twenty-five acres presented by the University of Oregon Medical School. This expansion will permit the housing of 300 patients as against 125 in the present leased structure. The pathologist service has been of especial value because of the diversity of autopsy material and the thoroughness of the case records. This will constitute the third hospital to be built on the same site, including already the Multnomah County Hospital and the Doernbecher Children's Hospital. The consulting pathologist of all these institutions is chosen from the department of pathology of the medical school.

Society News.—H. J. Corper has been elected president, E. D. Downing, vice president and D. N. Beacom, secretary-treasurer, of the Colorado Society of Clinical Pathologists.

Meeting of the German Pathological Society.—The next meeting of the German Pathological Society will take place in Danzig in the early part of June, 1926.

New Laboratories for Research at East Akron, O.—The Akron Lodge of Elks has built and equipped laboratories for research which have been given to the Springfield Lake Sanatorium, East Akron, O. Research in tuberculosis will be carried on by Dr. E. Crandall, resident physician, and others under the direction of Dr. E. E. Ecker, assistant professor of immunology at Western Reserve University.

Death of Edmund Krompecher.—Edmund Krompecher, professor of pathologic anatomy in the University of Budapest, whose work on cancer is well known, died recently.

Expedition to Central America for Parasitological Research.—The expedition to the tropics of Central America, organized by the Johns Hopkins School of Hygiene and Public Health and conducted under the auspices of the International Health Board, has returned. W. W. Cort, professor of helminthology, Johns Hopkins University, was the director, and among the members were Maurice C. Hall, chief of the zoological division of the U. S. Bureau of Animal Industry, W. A. Riley, of the University of Minnesota, and D. L. Augustine, of Harvard Medical School. Besides gathering much information on parasites and parasitic diseases in man and animals in the countries visited, the expedition brought back a large collection of the prevailing parasites, some of them apparently new and of economic and scientific importance. Important information with respect to tropical diseases likely to be carried northward by shipments of livestock was obtained. Observations were made that will be of value to public health work in those regions.

University News, Promotions, Resignations and Appointments.—Kenneth M. Lynch has returned to the chair of pathology in the Medical College of the State of South Carolina, Charleston, succeeding F. H. Dieterich, resigned.

At the University of West Virginia, Clement Coleman Fenton has been appointed professor of pathology and bacteriology in the place of William A. Smith, who has become pathologist at the Veterans Hospital, Outwood, Ky.

In the department of hygiene and bacteriology of the medical school of Western Reserve University, Ralph H. Heeren has been appointed instructor. Mildred Winchester and LaVerne Barnes have resigned as instructor and demonstrator in bacteriology, respectively, to accept positions in Washington State College at Pullman.

William E. Brown has been appointed assistant professor of industrial medicine on a full time basis in the department of bacteriology and hygiene at the Medical College of the University of Cincinnati. Dr. Brown (Harvard) holds the certificate in public health from the Massachusetts Institute of Technology where he was an instructor from 1915 to 1919; later he was surgeon-in-chief for the New Jersey Zinc Company.

Bernhard Steinberg, for two years fellow in medicine of the National Research Council, working in the department of pathology at Western Reserve University, has accepted an appointment of director of laboratories, Toledo Hospital, Toledo, Ohio.

Edward L. Saylor has been appointed resident pathologist to the Bell Memorial Hospital and assistant in the department of pathology of the University of Kansas School of Medicine.

Ferdinand C. Helwig has been appointed visiting pathologist to the Children's Mercy Hospital, Kansas City, Mo.

H. R. Wahl, professor of pathology in the University of Kansas, has been appointed visiting pathologist to the Bethany Hospital, Kansas City, Kan.

J. L. Goforth has resigned as senior resident pathologist at the Philadelphia General Hospital to take charge of the new laboratory of St. Paul's Sanitarium, Dallas, Texas, and his place has been taken by E. S. Clayton, former chief resident at the Lankenau Hospital, Philadelphia.

W. E. Chapin, formerly resident pathologist in the Pennsylvania Hospital, has been appointed assistant director of the laboratories of hygiene at the Municipal Hospital, Philadelphia.

R. S. Graham of the Lakeside Hospital, Cleveland, has been appointed resident pathologist in the Pennsylvania Hospital, Philadelphia.

Edward Bortz has been appointed assistant instructor in the department of pathology in the University of Pennsylvania.

Edgar R. Pund has been promoted to associate professor of pathology in the medical department of the University of Georgia at Augusta.

Coy C. Carpenter has been appointed professor of pathology at Wake Forest College in the place of F. W. Carroll, who resigned to engage in the practice of medicine.

In Cornell University Medical College, New York, James Denton has been appointed assistant professor in pathology, and pathologist in the New York Hospital, and C. T. Olcott, instructor in pathology.

Paul Klemperer, associate professor of pathology in New York Post-Graduate Medical School and Hospital, has resigned to accept the position of pathologist in Mt. Sinai Hospital, New York.

Ward Hance Cook has been appointed assistant professor of pathology in the New York Post-Graduate Medical School and Hospital.

Walter L. Kulp has been promoted to assistant professor, and Wayne M. Plastring has been appointed assistant, in general bacteriology at Yale University.

Third Annual Report of the Ella Sachs Plotz Foundation for the Advancement of Scientific Investigation.—During the third year of the Ella Sachs Plotz Foundation for the Advancement of Scientific Investigation thirty-eight applications for grants were received by the trustees. Fourteen of these came from eight different countries in Europe and Asia, and the others came from the United States. The total number of grants made was thirteen, two of these being to investigators to whom aid had been promised for two and three years respectively. Seven of the new grants were made to scientists in countries outside of the United States.

In the three years of its existence thirty-five grants have been made, and investigators have been assisted in the United States, Great Britain, France, Germany, Austria, Hungary, Switzerland and Esthonia. The list of investigators and of the researches which have been aided in the current year is as follows:

1. L. H. Newburgh, University of Michigan, \$1,250 a year for three years for a study of the production of chronic nephritis with high protein diets and amino acids.
2. William deB. MacNider, University of North Carolina, \$1,700 a year for two years for research in chronic experimental nephritis.
3. Henry G. Barbour and Glenn R. Spurling, University of Louisville, \$500 for investigation of operative and anesthetic shock.

4. Robert Chambers, Cornell University, \$500 for the continuation of the study of problems in cell physiology.

5. James E. Dawson, Edinburgh, Scotland, \$250 a year for two years, for investigation on the pathology of the breast.

6. Paul Hari, Budapest, Hungary, \$1,000 for study of diseases of the metabolism with special reference to diabetes in animals and man.

7. Warfield T. Longcope, Johns Hopkins Hospital, \$750 for studies on the etiologic relationship of streptococcus infections to acute and subacute nephritis.

8. David Marine, Montefiore Hospital for Chronic Diseases, \$1,200 for study of the inorganic salts of the body and their excretion following suprarenalectomy.

9. J. K. Parnas, University of Lwow, Lwow, Poland, \$500 for study of ammonia in blood.

10. Charles Richet, Paris, France, \$1,000 for research on tuberculosis.

11. Paul Saxl, Vienna, Austria, \$250 for research in immunity from infectious diseases.

12. C. R. Schlayer, Berlin, Germany, \$250 for studies on renal function and its relation to blood and tissue.

13. H. Siegmund, Koln-Lindenthal, Germany, \$250 for studies on the relation of antibody formation to the reticulo-endothelial system.

In their first statement regarding the purposes for which the fund would be used the trustees expressed themselves as follows:

1. For the present, researches will be favored that are directed toward the solution of problems in medicine and surgery or in branches of science bearing on medicine and surgery.

2. As a rule, preference will be given to researches on a single problem or on closely allied problems; it is hoped that investigators in this and in other countries may be found, whose work on similar or related problems may be assisted so that more rapid progress may be made possible.

3. Grants may be used for the purchase of apparatus and supplies that are needed for special investigations, and for the payment of unusual expenses incident to such investigations, including technical assistance, but not for providing apparatus or materials which are ordinarily a part of laboratory equipment. Stipends for the support of investigators will be granted only under exceptional circumstances.

In accordance with the policy outlined in statement 2, four of the investigations which have been aided in 1926 bear on the general subject of chronic nephritis; in 1925 there were four grants for work in this field, and in 1924 there were also four grants for work in the same field.

Applications for grants to be held during the year 1927-1928 should be in the hands of the executive committee before May 15, 1927, but if all the funds are not assigned in the spring, further consideration will be given to applications received before September 15.

Applications should include statements as to the character of the proposed research, the amount of money requested and the objects for which the money is to be expended.

Applications should be sent to the secretary of the executive committee, Dr. Francis W. Peabody, Boston City Hospital, Boston.

DOCTORATES IN MEDICAL SCIENCES CONFERRED BY
AMERICAN UNIVERSITIES, 1925-1926

Callie Hull and Clarence J. West, Research Information Service,
National Research Council, Washington, D. C.

The following list of doctorates in Anatomy, Bacteriology, Pathology and Physiology (including Physiologic Chemistry) granted during the academic year 1925-1926, has been compiled from information supplied through the courtesy of the various American universities granting the doctor's degree. A similar list covering the years 1922-1925 was published in the ARCHIVES 1:259-262 (Feb.) 1926. It is offered again as a suggestive guide to the research work which is being carried on at different universities, and to the persons interested in special fields of investigation.

ANATOMY

Chicago: Theophil Paul Grauer, "Regeneration in the Pancreas of the Rabbit." John C. Rogers, "The Fate of Human and Avian Tubercle Bacilli in the Liver of Birds."

Kansas: Armando W. Angulo y Gonzales, "Spinal Motor Nuclei." Ira D. Hogg, "A Description of the Motor Nuclei of the Cranial Nerves of *Mus Norvegicus Albinus* at the Time of Birth."

Minnesota: William Thomas Peyton, "Developmental Topographical Anatomy of the Head and Neck of the Fetus, the Newborn, the Child and the Adult as Determined by the Orthoscopic Method." Roy Edwin Swanson, "The Growth of the Human Female Pelvis from Birth to Maturity: a Graphic and Quantitative Study."

Northwestern: William Frederick Windle, "Studies on the Trigeminal Nerve with Particular Reference to the Pathway for Painful Afferent Impulses."

Stanford: Earl Theron Engle, "A Morphological and Experimental Study of the Coagulatory Gland of the Guinea-Pig, *Cavia Cobaya*."

Washington University, St. Louis: Sam Lillard Clark, "Nissl Granules of Primary Afferent Neurones."

BACTERIOLOGY

Catholic: John Joseph Clarke, "A Study of Thermophilic Bacteria in Pasteurized Milk." Joseph Mary Dougherty, "A Study of Thermophilic Bacteria in Pasteurized Milk."

Chicago: Lee Miles Roderick, "Studies in Food Spoilage." Allan Funder Reith, "Bacteria in the Muscles and Blood of Apparently Normal Animals."

Cincinnati: John Henry Highberger, "Bacterial Physiology in Relation to Goatskins."

Columbia: Rebecca Craighill Lancefield, "The Immunological Relationships of *Streptococcus Viridans* and Certain of Its Chemical Fractions."

Cornell: Harold Raymond Curran, "The Growth of Bacteria."

Iowa State College: John C. Weldin, "The Colon-Typhoid Group of Bacteria and Related Forms: Relationships and Classifications."

Kansas: Elbert Lee Treece, "Cultural and Metabolic Studies of the Colon-Aerogenes Group of Bacteria."

Massachusetts Agricultural College: Joseph Raymond Sanborn, "Physiological Studies in Cellulose Fermentation."

Pennsylvania: William Alfred Kreidler, "Bacteriologic Studies in Endocarditis."

Radcliffe: Dorothea Eggleston Smith, "Studies in the Capsular Substance of Bacteria, with Reference to Virulence."

Wisconsin: John Arlington Anderson, "Biochemical Studies on Certain Soil Bacteria."

Yale: Algot Reginald Nelson, "Bacteriophagy in Cellular Immunity." Morris Louis Rakieten, "Studies with Brilliant Green with Special Reference to an Improved Enrichment Method for Isolating Typhoid and Para-Typhoid Bacilli." Edward Freeman Roberts, "The Relation of the Reticulo-Endothelial System to Antibody Production." Howard John Shaughnessy, "The Effect of Bacterial Cells upon the Chemical Composition of a Surrounding Menstruum as Influenced by the Presence of Various Electrolytes." Charles Arthur Slanetz, "The Influence of Phosphate Buffer on Bacterial Metabolism in Carbohydrate-free and in Glucose-containing Media." George Valley, "The Effect of Carbon Dioxide on Bacteria." Elliot Ross Weyer, "A Bacteriological Study of the Microorganism Commonly Concerned in the Production of Butyl Alcohol and Acetone by the Biological Process."

PATHOLOGY

American University: Grover Cleveland Kirk, "The Comparative Constitutional Resistance to Pulmonary Tuberculosis Manifested by the Various Personality Reaction Tests."

Johns Hopkins: Persis Putnam, "Sex Differences in Pulmonary Tuberculosis Deaths." Howard Bancroft Andervont, "The Relationship of the Epithelioma Contagiosum Virus of Fowls to the Vaccine Virus."

Pennsylvania: Raymond Sears Patterson, "A Study of the Laboratory Aids to the Diagnosis of Chronic Neisserian Infection."

PHYSIOLOGY

Boston: Burnham Sarle Walker, "A Study of Renal Excretion with Special Reference to Ambard's Laws."

California: George Frank Pilz, "The Relation of the After-Nystagmus to the Rotation-Nystagmus."

California Institute of Technology: Gordon Alles, "The Comparative Physiological Action of Some Guanidine Derivatives."

Catholic: John William Rauth, "Variations in the Constitution of the Blood in Psychotic Patients."

Chicago: Margaret Stella Chaney, "The Effect of Orange Juice on the Metabolism of Two Growing Children: I. Calcium, Phosphorus, Magnesium and Nitrogen Metabolism. II. Urinary Organic Acids, Ammonia and Hydrogen Ion Concentration." Hsi Chun Chang, "Studies on the Physiology of the Thyroid Gland." Kate Daum, "I. The Effect of Heat Upon Certain Constituents of Milk. II. Adult Utilization of Heated Milk." Marietta Eichelberger, "The Effect of Light on Creatinine Excretion and Basal Metabolism." Martha Belle Farnum, "The Effect of the Production of Beriberi on Gastric Secretion." Harold Clifford Goldthorpe, "In Vitro Studies on Ammonia and Urea Formation by Tissues." Reuben Gilbert Gustavson, "A Biochemical Study of the Female Sex Hormone." Frederic Theodore Jung, "On the Existence of a Parathyroid Hormone." Edmund Joseph Jurica, "Studies on the Motility of the Denervated Mammalian Esophagus." Thomas Leroy McMeekin, "Studies on the Purification of Pepsin." Carlos Isaac Reed, "Studies on the Physiological Action of Light." Sarah Sheldon Tower, "A Study of the Sympathetic Innervation to Skeletal Muscle."

Cornell: William Ernest Krauss, "The Non-Protein Nitrogen in Certain Dairy Rations and the Partition of Nitrogen in the Urine Produced Thereon." Russell Cooper Miller, "A Study of Calcium and Phosphorus Balances with Dairy Cattle."

Harvard: Lawrence Rogers Blinks, "The Permeability and Electrical Conductivity of Single Cells." Charles Julius Lyon, "The Role of Phosphate in Plant Respiration." Laurence Hasbrouck Snyder, "Human Blood Groups: Their Inheritance and Racial Significance."

Iowa State University: Emma Louise Wardell, "The Influence of the Ingestion of Methylated Purines on the Excretion of Uric Acid."

Johns Hopkins: Emil Bogomir Cekada, "The Preparation and Properties of Prothrombin." Francis Marion Walters, "Effects of Carbon Monoxide Poisoning Upon Metabolism." Lois Emily Witham, "Some Studies on the Chemical Nature of Vitamin B and a Comparative Study of the Vitamin B Requirements of Rats and Pigeons."

Michigan: Detlev Wulf Bronk, "An Electrometric Study of the Submaxillary Gland of the Dog." Seiichi Izume, "Studies on the Influence of Hydrazine, Substituted Hydrazines and Related Nitrogenous Compounds on the Carbohydrate Metabolism in the Rabbit."

Minnesota: J. Roy Haag, "The Antagonism of Mineral Ions in Animal Nutrition."

Missouri: Harold McCloskey Harshaw, "A Study of the Nutrients Required by Mammals for Successful Reproduction."

Ohio State: Fred Andrews Hitchcock, "Studies on Vigor and Growth of the White Rat." Milton Oliver Lee, "Studies on the Oestrous Cycle in the White Rat."

Pennsylvania: Mary Adelia Bennett, "Studies on Hemorrhage." Stanley Elphinstone Kerr, "Studies on the Inorganic Composition of Blood."

Radcliffe: Abby Howe Turner, "The Evaluation of Circulatory and Respiratory Efficiency in Normal Young Women."

Stanford: Lois Lockard MacKay, "A Study of the Effect of Various Factors on the Rate and Degree of Compensatory and Simple Hypertrophy of the Kidney."

Wisconsin: Merle Starr Nichols, "Studies on the Metabolism of *Corynebacterium Diphtheriae*." Robert William West, "The Nature of Vocal Sounds."

Yale: Harold Levine, "Some Effects of Unusual Diets upon Growth, Exercise, and Metabolism, with Special Reference to Ketosis in the Rat." Mary Clarissa McKee, "Some Nitrogenous Constituents of the Cauliflower." George Albert Williams, "A Study of the Laxative Action of Wheat Bran." Jet Corine Winters, "The Effects of Dietary Deficiencies on the Growth of Certain Body Systems and Organs." Mildred Ruth Ziegler, "An Investigation of the Excretion of Organic Dyes: A Study of Membrane Permeability."

Doctorates Conferred in Medical Sciences, 1925-1926

	Anatomy				Bacteriology				Pathology				Physiology			
	1922 and 1923	1923 and 1924	1924 and 1925	1925 and 1926	1922 and 1923	1923 and 1924	1924 and 1925	1925 and 1926	1922 and 1923	1923 and 1924	1924 and 1925	1925 and 1926	1922 and 1923	1923 and 1924	1924 and 1925	1925 and 1926
American University...	1
Boston.....	1
Brown.....	2	1	1
California.....	1	1	1
California Institute of Technology.....	1
Catholic.....	2	1	1
Chicago.....	3	2	2	2	5	3	1	2	1	6	4	3	3	12
Cincinnati.....	1	1	1
Columbia.....	1	4	1	1	3
Cornell.....	1	1	2	..	1	1	..	1	2	1	2
George Washington....	2	1	..
Harvard.....	1	1	1	1	3
Illinois.....	2	..	1	1	1
Iowa.....	1	1
Iowa State.....	1	1
Johns Hopkins.....	7	..	6	..	7	3	4	2	..	2	..	3
Kansas.....	1	2	..	1	..	1
Massachusetts Agricul- tural College.....	1
Michigan.....	2	1	2
Minnesota.....	4	1	1	2	1	..	3	1
Missouri.....	1	2	1
New York.....	1	1
Northwestern.....	1	1	2
Ohio State.....	1	2
Pennsylvania.....	1	1	1	2
Radcliff.....	1	1	1
Stanford.....	1	2	..	1
Washington University, St. Louis.....	..	1	..	1
Wisconsin.....	2	1	4	1	3	1	..	2
Yale.....	4	2	6	7	2	3	..	1	5
Total.....	10	4	4	9	30	13	20	20	11	11	5	4	19	17	13	42

Abstracts from Current Literature

Pathologic Physiology

A NEW FORM OF CONGENITAL HEMATOPORPHYRIA: OLIGOCHROMEMIA PORPHYRINURIA (MEGALOSPLENICA CONGENITA). AKIRA SATO and HIROSHI TAKAHASHI, *Am. J. Dis. Child.* **32**:325, 1926.

This congenital and familial disease is characterized by porphyria and consequent sensitiveness to light from birth, by enlarged spleen, by a chlorotic form of anemia, and by a fatal course. The cases in the literature are reviewed and a typical instance described in a boy who died at the age of 15 months.

EXPERIMENTAL STUDIES ON THE TOXEMIAS OF PREGNANCY. CAN HISTAMINE BE REGARDED AS THE ETIOLOGIC FACTOR? J. HOFBAUER, *Am. J. Obst. & Gynec.* **12**:159, 1926.

Hofbauer reports interesting experimental data on the effects of histamine in various doses on pregnant animals. A picture suggestive of premature separation of a normally implanted placenta is reproduced in guinea-pigs. In carnivorous animals two phenomena can be observed: changes similar to pernicious vomiting if histamine is administered over prolonged periods of time, and changes in the liver and kidneys similar to those seen post mortem in women who died of eclampsia. The changes in tension noted in eclampsia may be due to alterations in the vasomotor centers or in the potassium and calcium ratio, the calcium decrease being counterbalanced by epinephrine. There is a striking similarity of the blood chemical changes in eclampsia and acute histamine intoxication. The kymographic tracing of the guinea-pig uterus treated with eclamptic blood serum is identical with that caused by histamine. Hofbauer suggests that the source of histamine in the blood of eclamptic patients may be found in the breaking down of the syncytial buds into toxic split products which may be taken up into the maternal circulation.

A. J. KOBAK.

A STUDY OF BASAL METABOLISM AND BLOOD CHEMISTRY FOLLOWING BILATERAL OÖPHORECTOMY. S. GEIST and M. GOLDBERGER, *Am. J. Obst. & Gynec.* **12**:206, 1926.

Geist and Goldberger find that removal of both ovaries does not give rise to consistent variation in basal metabolism or body weight. It was also noted that there were no definite relationships between the variations in weight and basal metabolism and that the blood chemistry and blood pressure remained uninfluenced by this operation.

A. J. KOBAK.

ON DIMINISHED RESISTANCE FOLLOWING SUPRARENALECTOMY IN THE RAT AND THE PROTECTION AFFORDED BY AUTOPLASTIC TRANSPLANTS. HENRY L. JAFFE, *Am. J. Path.* **2**:421, 1926.

The removal of both suprarenals in rats invariably leads, in the absence of gross accessory tissue, to loss of resistance to typhoid vaccine. This effect is caused by loss of some function of the cortex. Hypertrophied accessories may protect against fatal doses of vaccine after suprarenalectomy, and auto-

plastic cortical transplants may protect animals which do not have any other suprarenal tissue. Suprarenlectomized rats show also lowered resistance of natural infection.

PULMONARY ACTIVITY GREATEST AT THE APEX AND LEAST AT THE BASE. J. WALSH, *Am. Rev. Tuberc.* **14**:142, 1926.

Microscopic study shows that the alveoli in the lung of a new-born baby are practically all of the same size and that they enlarge with age, the increase being greatest at the apex and least at the base. In the adult the alveoli are larger in the apex than in the base, larger in the central portions of the lung than near the pleural surface. When the size of the alveoli is pathologically increased in emphysema, again the largest size is found in the apex and the least distention in the base. In generalized miliary tuberculosis the tubercles decrease generally in size and numbers in craniocaudal direction. Anthracosis likewise decreases in intensity from apex to base. Tuberculous foci in the lower parts of the lung have a greater tendency to heal by fibrosis, as evidenced by the almost universally occurring healing of the primary focus, which is only rarely found in the apical portions, as contrasted with the tendency to progression of apical lesions. When a clinical lesion heals, râles and roentgenologic signs disappear from below upward. The predilection of the lower parts of the lung for edema and hypostasis points to the fact that these parts, and not the apexes, have the least active blood circulation. If the predominance of tuberculous lesions in the apex is to be explained by the oxygen requirement of the tubercle bacillus, one must necessarily conclude that the apexes are better areated than the rest of the lung. Where the lymph flow is greatest in the lung is an undecided question. Walsh thinks that "the bacilli of a primary 'affect,' whether this is under the skin or in the lung, or at the apex, base, or mid lung where it usually is, are picked up by the lymph vessels and carried to the nearest lymph nodes where they produce a lesion; the bacilli of the secondary manifestation are not picked up by the lymph vessels at all. This being true, it matters not whether the lymph drainage is greater or less. Tubercle bacilli will not be washed out by it." All these observations, supported by therapeutic results from rest, and by the fact that the apexes lack protection, led Walsh to the conclusion that the functional activity—contrary to the generally accepted views—is greatest at the apex. This explains the usual craniocaudal development of clinical pulmonary tuberculosis, chronic hypertrophic emphysema and anthracosis, and the preference for lobar pneumonia to localize in the lower parts, where the respiratory activity is least and the circulation becomes more readily stagnant.

MAX PINNER.

THE PATHOGENESIS OF LIPOID NEPHROSIS. H. ELWYN, *Arch. Int. Med.* **38**:346, 1926.

The main features of lipid nephrosis are: albuminuria, oliguria, edema, diminution in the total protein of the blood with a diminution in the albumin fraction and the relative and absolute increase in the globulin fraction, increase in the cholesterolin of the blood, lowering of the basal metabolic rate, a practically protein-free edema fluid and the deposit of lipoids in the cells of the kidney tubules. The disease occurs either alone or in combination with diffuse glomerulonephritis or with amyloid disease. The first symptom in the cases that can be observed from the beginning is the albuminuria. The albuminuria is the result of a more or less persistent injury to the glomerular and capsular

epithelium by a previous acute diffuse nephritis that has subsided. When lipid nephrosis accompanies amyloid degeneration the injury to the glomerular and capsular epithelium is caused by the toxins of the disease that are responsible for the amyloid deposit. The oliguria is the result of a regulative effort on the part of the organism to prevent loss of protein. The absolute increase of the globulin fraction in the blood is the result of a regulative effort on the part of the organism in an attempt to conserve the proteins of the blood by replacing the lost albumin with a protein of a larger molecular aggregate, hence one that passes less easily through the injured glomerular filter. The edema is the result of a regulative effort on the part of the organism in an attempt to maintain the normal blood volume. Since one of the gates by which the excess of fluid is eliminated, namely, the kidneys, is less active, there is danger that the fluid volume of the blood will be increased. This is obviated by the formation of edema. To prevent the escape of the plasma protein into the edema fluid, the capillaries become less permeable by increased contraction. The result is pallor, and a diminution in the supply of nutrition and of oxygen to the tissues and organs. This diminution results in a disturbance of intracellular oxidation and of the proper utilization of foodstuffs. The result is a lowered metabolic rate, loss of flesh and a diminished resistance to infection. The diminution of the utilization of nutrition also results in an increase of lipoids in the cells, and later in the blood, with the production of a hypercholesterinemia. The lipoids of the blood pass through the injured glomerular filter and from the filtrate add themselves to the lipoids already present in the cells of the kidney tubules. They also appear in the urine. The main features of lipid nephrosis are thus considered from the point of view of regulation in an effort on the part of the organism to compensate for the loss of protein and to prevent a greater loss. The possibility that the pneumococcus may be a causative factor in the production of the acute nephritis that precedes the development of lipid nephrosis must be considered. Its continued presence in the kidney is possibly responsible for its occasional invasion of the peritoneal cavity, and the development of peritonitis.

S. A. LEVINSON.

THE BASAL METABOLIC RATE IN CASES OF CHRONIC CARDIAC DISEASE AND IN CASES OF HYPERTENSION. S. SHAPIRO, *Arch. Int. Med.* **38**:385, 1926.

The results are practically the same as those of Peabody, DuBois and their associates. The metabolic rates of persons with organic heart disease, including those with hypertension and cardiac hypertrophy, obtained under basal conditions, fall within the accepted normal limits. High readings are usually due to dyspnea. Cardiac overactivity such as in a heart compensating for an organic defect or maintaining an elevated vascular tension does not detectably elevate the heat production.

S. A. LEVINSON.

SCROTAL REPLACEMENT OF EXPERIMENTAL CRYPTORCHID TESTES AND THE RECOVERY OF SPERMATOGENETIC FUNCTION (GUINEA-PIG). CARL L. MOORE, *Biol. Bull.* **51**:112, 1926.

Guinea-pig testes elevated from the scrotum to the abdomen shortly after birth (prespermatogenic) will, if opposed by a normal testis, retain an undifferentiated character practically throughout the life of the animal. If unaccompanied by a normal testis, they undergo changes leading to the enlargement of

seminiferous tubules lined with cells of Sertoli, relative increase of interstitial cells and a general condition unlike that of the embryonic type.

Replacement in the scrotum of the testis retained in the abdomen for five months was followed by normal activity and differentiation of spermatozoa in eight of nine cases. Presumably normal development of abdominal testes confined in the abdomen for much longer periods followed scrotal replacement.

Spermatozoa are produced in the testis within ninety days after scrotal replacement.

Development of the replaced testis occurs in the presence or absence of an opposite normal testis.

By implication we are led to believe that congenitally retained abdominal testes in man have a good chance to develop into normal testes if they are replaced in the scrotum at a time considerably after the attainment of sexual maturity.

The function of the scrotum is well shown by comparison of the testis retained in the abdomen for several months with a similar testis replaced in the scrotum for ninety days. Only in the scrotum are spermatozoa produced in the testes.

AUTHOR'S SUMMARY.

THE FATE OF THE GERMINAL EPITHELIUM OF EXPERIMENTAL CRYPTORCHID TESTES OF GUINEA-PIGS. WALTER LAWRENCE, *Biol. Bull.* 51:129, 1926.

When the testes of sexually mature male guinea-pigs are elevated to and allowed to remain in the abdominal cavity, a progressive desquamation and degeneration of the germinal epithelium takes place; at six days abdominal retention degeneration is well marked, at ten days well advanced, and at twenty days practically all epithelium has been removed. This degeneration can be attributed directly to the increased temperature of the abdominal cavity over that of the scrotum.

Neither the speed nor the nature of the degenerative process is effected by ligation of the ductus deferens of the cryptorchid testis.

All of the degenerating elements from the seminiferous tubules are absorbed in the testis proper or are carried to the epididymis, where they are absorbed with the greater part of the spermatozoa which were present at the time the testis was elevated to the abdominal cavity.

Absorption of the germinal epithelium from a cryptorchid testis into the blood stream does not affect the integrity of the scrotally retained normal testis.

Spermatozoa will remain alive in the germinal passages of the guinea-pig for more than nine days. Following their loss of motility, they rapidly lose their tendency to clump; but degeneration of mature spermatozoa occurs slowly, especially so in the ductus deferens. It has been determined that a given spermatozoon in the male genital passages though retaining its capacity for motility for nine days, may retain its morphologic identity for more than 100 days.

Venous stasis through ligation of the internal spermatic vein of testes allowed to remain in the scrotum does not produce the degeneration complex seen in testes retained in the abdominal cavity.

AUTHOR'S SUMMARY.

ACUTE NEPHRITIS IN CHILDREN, WITH SPECIAL REFERENCE TO THE TREATMENT OF UREMIA. KENNETH D. BLACKFAN, *Bull. Johns Hopkins Hosp.* 39:69, 1926.

The following points are emphasized. The form of uremia seen in acute glomerular nephritis in children is usually preceded by a steady rise in

arterial tension and by visible but not necessarily marked edema. Intracranial tension resulting from edema of the brain is probably the causative factor of the symptoms in this form of uremia. Arterial hypertension is probably the result of increased intracranial pressure.

The intravenous injection of 1 per cent solution of magnesium sulphate together with the administration of large doses of the salt by mouth and by rectum has been found to be effective in the treatment of this form of uremia.

Intravenous treatment is not effective during the medullary cone phase or in the terminal stages. Lumbar puncture should be used guardedly in order to avoid incarceration of an edematous brain in the foramen magnum. It is suggested that the characteristic symptoms with arterial hypertension be referred to as the cerebral symptoms of acute glomerular nephritis.

AUTHOR'S SUMMARY.

LACTIC ACID IN THE TOXEMIAS OF PREGNANCY. H. J. STANDER and A. H. RADELET, *Bull. Johns Hopkins Hosp.* **39**:91, 1926.

In pregnancy complicated with a low amount of reserve power of the kidney to eliminate, the lactic acid in the blood is increased. This accumulation of lactic acid disappears as the patient improves. In pregnancy complicated with nephritis, there is a similar accumulation of lactic acid in the blood, which disappears with the improvement of the patient. The factors which may possibly play a rôle in the accumulation of lactic acid in these two types of pregnancy toxemia are: (a) decreased elimination of lactic acid; (b) decreased oxidation and interference with the resynthesis of lactic acid into glycogen; (c) a possible disturbance of the hydrogen ion concentration of the blood.

AUTHORS' SUMMARY.

THE INFLUENCE OF CHANGES IN THE HYDROGEN ION CONCENTRATION UPON THE REFRACTORY PERIOD OF THE PERFUSED MAMMALIAN HEART. E. P. CARTER and F. R. DIEUAIDE, *Bull. Johns Hopkins Hosp.* **39**:99, 1926.

It is apparent that with a change only in the hydrogen ion concentration of the perfusion fluid throughout so narrow a range as pH 7 to 7.8, there follows an abrupt and significant alteration in the refractory period of both auricular and ventricular muscle of the dog's heart when perfusion is performed, the refractory period being lengthened with the acid and shortened with the alkaline perfusate.

The importance of this alteration in the duration of the refractory period in relation to re-entrant waves, circus movements and changes in the transmission interval in cardiac muscle suggests itself and is to be emphasized.

It is conceivable that in the myocardium, the seat of local disease processes in man, such regional changes in the hydrogen ion concentration may occur as to modify the refractory period of the tissue involved, leading to disturbances in the normal sequence of events as suggested above.

AUTHORS' SUMMARY.

FORMATION OF TOXIC FLUID IN ISOLATED DUODENOJEJUNAL LOOPS. LOUIS BRAEYE, *Bull. Johns Hopkins Hosp.* **39**:121, 1926.

Ten hours is the minimal time required for the formation of an appreciable amount of fluid; this accumulation can cause gangrene as early as twenty

hours after obstruction. As a rule, more than thirty-six hours are required to develop toxic properties. The fatal dose for a small dog is 25 cc., injected intravenously.

INVESTIGATIONS IN TETANY. P. DRUCKER and F. FABER, *J. Biol. Chem.* **68**:57, 1926.

The p_H values are not more alkaline nor is the alkali reserve greater when tetany is manifest than when it is cured. It is improbable that hypocalcemia and tetany are the consequence of an alkalosis.

ARTHUR LOCKE.

THE EFFECT OF EXCRETION OF ACIDS AND BASES UPON THE DEVELOPMENT OF ACIDOSIS IN EXPERIMENTAL DIABETES. B. M. HENDRIX, M. FAY, D. B. CALVIN and M. BODANSKY, *J. Biol. Chem.* **69**:449, 1926.

Acidosis develops in depancreatized dogs only when the volume of excreted urine becomes relatively large.

ARTHUR LOCKE.

BLOOD CHOLESTEROL DURING ETHER ANESTHESIA. A. MAHLER, *J. Biol. Chem.* **69**:653, 1926.

Patients receiving ether anesthesia show a rise in total blood cholesterol which is proportional to the rise in blood glucose and the duration of anesthesia. This rise is prevented if insulin is administered several hours before anesthesia is begun. Insulin appears to be one of the factors controlling the cholesterol content of the blood, and its secretion may be partially suppressed during ether anesthesia.

ARTHUR LOCKE.

SOME CHANGES IN THE ACID-BASE EQUILIBRIUM OF THE BLOOD CAUSED BY HEMORRHAGE. M. A. BENNETT, *J. Biol. Chem.* **69**:675, 1926.

Blood was studied at various intervals after large hemorrhages in dogs. After hemorrhage there was a rapid acid production as indicated by a fall in p_H and alkaline reserve. The alkaline reserve started to rise quickly and was normal on the day following the hemorrhage. At this time the p_H had swung to the alkaline side of normal. It returned to normal after several days. The observations are discussed from the point of view of several recent theories concerning the regulation of blood alkali and the activity of the respiratory center.

AUTHOR'S SUMMARY.

PHOSPHATE METABOLISM AS RELATED TO ANESTHESIA. A. BOLLIGER, *J. Biol. Chem.* **69**:721, 1926.

Ether chloroform and ethylene gas, and oxygen anesthesia, well administered and uncomplicated, depress the inorganic phosphates. Morphine and atropine mask effects of anesthesia on metabolism because they themselves produce changes. The early recovery period from anesthesia is marked by blood phosphates well below the fasting level, and the excretion of phosphates is low or ceases altogether. Complications such as asphyxia, excessive muscular exertion, or morphine may mask or reverse the trend of phosphate metabolism. The depression of the blood phosphates occurring with lowered carbon dioxide capacity and p_H shows that there is no relation between the increased acidity

and the phosphate content of the blood. The absence of variation in the inorganic blood phosphate curve during anesthesia in the depancreatized dog, however, suggests the close relation with carbohydrate metabolism.

AUTHOR'S SUMMARY.

UTILIZATION OF CARBOHYDRATES IN A CASE OF CHRONIC PENTOSURIA. I. M. RABINOWITCH, *J. Clin. Investigation* 2:457, 1926.

The view is confirmed that in chronic pentosuria the utilization of carbohydrates is unimpaired. So far as their carbohydrate metabolism is concerned, there is no reason for restricting the diet of pentosuric patients or for classifying them as substandard insurance risks.

THE PREVENTION OF PIGMENT FORMATION IN THE HAIR FOLLICLES OF COLORED MICE WITH HIGH VOLTAGE X-RAY. ROBERT T. HANCE and JAMES B. MURPHY, *J. Exper. Med.* 44:339, 1926.

Hard roentgen rays prevent the formation of pigment in the hair follicles of mice, with the result that hair previously black comes in white. Exposure of the ventral side of a mouse to the roentgen rays causes the hair on the back to come in white about forty to fifty days after it has whitened the hairs on the abdomen.

AUTHORS' SUMMARY.

ACTION ON FIBROBLASTS OF THE PROTEIN FRACTION OF EMBRYONIC TISSUE EXTRACT. LILLIAN E. BAKER and ALEXIS CARREL, *J. Exper. Med.* 44:387, 1926.

Fractionation of embryo tissue juice has shown that it is the protein fraction that contains the activating substance. Tissue continues to grow for a long time in the protein of the extract precipitated by carbon dioxide and at a rate approximately equal to that in the original extract diluted to the same nitrogen concentration. The nonprotein nitrogen gives slight stimulation to growth. Purification of the protein by repeated precipitation destroys its growth-promoting properties, but whether this is due to a denaturing of the protein—which occurs very readily—or to loss of some substance possibly an enzyme attached to it, has not been ascertained. Preparations of purified proteins from embryonic tissue and egg white have shown no marked nutritive or stimulating action. A number of other pure substances have been tried without effect.

AUTHORS' SUMMARY.

EFFECT OF THE AMINO ACIDS AND DIALYZABLE CONSTITUENTS OF EMBRYONIC TISSUE JUICE ON THE GROWTH OF FIBROBLASTS. LILLIAN E. BAKER and ALEXIS CARREL, *J. Exper. Med.* 44:397, 1926.

The ultrafiltrable constituents of embryonic tissue extract are unable to support cell life in vitro. They stimulate cell migration and possibly multiplication, without increasing the mass of the tissue. Embryonic tissue extract freed from amino acids by dialysis still retains a considerable part of its growth-promoting properties. The area of growth of tissues in embryonic tissue extract free from amino acids is appreciably less than that with the whole extract, probably owing to the denaturation of part of the protein, or

perhaps to the inactivation or loss of an enzyme. The addition of either the unfiltrable components or an artificial mixture of amino acids to this dialyzed extract increases the area of cell migration but does not restore all the activity lost on dialyses. The observed differences in growth of tissue, due to the addition or removal of dialyzable and ultrafiltrable constituents of the extract, prove that the amino acids produce a more active cell migration and possibly multiplication, but no building up of new protoplasm.

AUTHORS' SUMMARY.

THE VISCOSITY OF THE BLOOD OF THE DOG AFTER OBSTRUCTION OF THE UPPER GASTRO-INTESTINAL TRACT. RUSSELL L. HADEN and THOMAS G. ORR, *J. Exper. Med.* **44**:419, 1926.

SURFACE TENSION OF THE BLOOD SERUM OF THE DOG AFTER UPPER GASTRO-INTESTINAL TRACT OBSTRUCTION. *Ibid.*, p. 425.

THE SEDIMENTATION RATE OF THE ERYTHROCYTES IN EXPERIMENTAL OBSTRUCTION OF THE GASTRO-INTESTINAL TRACT. *Ibid.*, p. 429.

THE CHLORIDE CONTENT OF THE TISSUES OF THE DOG AFTER EXPERIMENTAL GASTRO-INTESTINAL TRACT OBSTRUCTION. *Ibid.*, p. 435.

With cardiac obstruction there is a rapid and marked rise in the viscosity of the whole blood and some increase in the viscosity of the plasma. The changes after pyloric obstruction are similar to those observed after cardiac obstruction. After obstruction of the upper jejunum only slight changes are observed. The increase in viscosity parallels closely the degree of the toxemia. It is unaccompanied by any marked concentration of the blood.

After obstruction of the upper gastro-intestinal tract the surface tension of the blood serum of the dog shows no marked change. There is a tendency of the time-drop to increase twenty-four hours after operation. There is no characteristic course of the time-drop.

After obstruction of the cardiac end of the stomach, of the pylorus and of the jejunum, the red cells separate from the plasma much more rapidly than normal. The variation in sedimentation time is due to a variation in the physiochemical status of the blood.

After obstruction of the pylorus there is a marked fall in the chloride content of the liver, and a slight fall in the muscle. Similar changes are observed after obstruction of the jejunum. With obstruction of the cardiac end of the stomach, no change was observed.

AUTHORS' SUMMARY.

PRESENT STATUS OF OUR KNOWLEDGE OF THE ETIOLOGY OF PELLAGRA. JOSEPH GOLDBERGER, *Medicine* **5**:79, 1926.

It is concluded from the evidence at hand that pellagra is caused by a faulty diet. The primary dietetic fault appears to be of the nature of a deficiency of a factor P-P, very probably, but not certainly, identical with a dietary essential, heretofore included under vitamin B, which some workers have attempted to identify with bios.

FEVER, INFECTIONS AND THE THYROID-ADRENAL APPARATUS. W. CRAMER, *Brit. J. Exper. Path.* **7**:95, 1926.

Cramer has previously demonstrated that thyroid and suprarenal glands form a humoral apparatus concerned in heat regulation of the body; increased activity

of these glands increases heat production and diminishes heat loss, so that fever is produced. Aseptic fever is the result of certain pathologic conditions involving hyperactivity of these two glands. When thyroid and suprarenal glands are particularly susceptible to bacterial toxins and exhaust these glands, they are known as "adrenaltotoxic" and "thyreotoxic" effects; when action is stimulating, they are known as "adrenaltotonic" and "thyreotonic" effects. The former effect is accompanied by subnormal temperature. The latter by fever.

S. A. LEVINSON.

CARBOHYDRATE METABOLISM IN DIPHTHERIA. FRANCIS J. HECTOR, *Lancet* 2:642, 1926.

In severe diphtheria, during the toxemia and acidosis, carbohydrate metabolism is disturbed; fasting blood sugar is abnormally low, and the ability of the tissue to utilize glucose is diminished.

THE FATE OF THE SUGAR DISAPPEARING UNDER THE ACTION OF INSULIN. C. H. BEST, J. P. HOET and H. P. MARKS, *Proc. Roy. Soc. B* 100:32, 1926. OXIDATION AND STORAGE OF GLUCOSE UNDER THE ACTION OF INSULIN, *ibid.*, p. 55. OBSERVATIONS ON THE ONSET OF RIGOR MORTIS. J. P. HOET and H. P. MARKS, *ibid.*, p. 72. ADDITIONAL NOTE ON THE EFFECT OF INSULIN ON THE LACTACIDOGEN CONTENT OF THE SKELETAL MUSCLES. C. H. BEST and H. P. MARKS, *ibid.*, p. 171.

"The disappearance under insulin of inorganic phosphate from the blood of the eviscerated spinal preparation is related to the disappearance of sugar, and not to the fall in sugar concentration in the blood. No significant portion of the sugar which disappears from the blood of this preparation, under the influence of insulin, is stored in the muscles as a phosphoric ester. When an abundance of sugar is available, a large proportion of the sugar which disappears from the blood of the spinal cat is deposited as glycogen in the skeletal muscles of the animal. Insulin hypoglycemia, lasting for from one to three hours, does not appreciably lower the glycogen content of the resting skeletal muscles of the spinal cat. The decrease or complete disappearance of the muscle glycogen of normal rabbits, produced by large doses of insulin, is chiefly due to the convulsions.

"The glucose which disappears from an eviscerated spinal preparation under the action of insulin is equal to the sum of the glycogen deposited in the muscles and the glucose-equivalent of the oxygen absorbed. This balance is preserved, whether the blood sugar is maintained at a high level by rapid infusion of glucose, or allowed to sink to a very low level by restricting the supply. The view is advocated that the effects of insulin in excess represent an intensification of its physiological effects.

"The precipitate rigor mortis observed in rabbits, dying after hypoglycemic convulsions or after prolonged thyroid feeding, is not due to the accumulation of lactic acid, nor to increased acidity of the muscle. The absence of glycogen and the decrease in lactacidogen of the muscle are the determining factors of this rigor. The mechanism of rigor mortis is discussed."

AUTHORS' SUMMARY.

THE HEAT PRODUCTION OF NERVES. A. C. DOWNING, R. W. GERARD and A. V. HILL, *Proc. Roy. Soc. B* **100**:223, 1926.

A detailed description is given of a new apparatus and method for the accurate measurement of the heat production of isolated nerve tissue. The total heat produced by 1 gram of nerve tissue per second of stimulation is about 7×10^{-5} calories. Ninety per cent of this heat is liberated within a period of from nine to eleven minutes after the cessation of the stimulus.

ARTHUR LOCKE.

THE EXCRETION OF URIC ACID BY THE KIDNEY. H. GREMELS and R. BODO, *Proc. Roy. Soc., Series B*, **100**:336, 1926.

The concentration of uric acid in the urine is dependent on the related concentration in the blood and on the rate of urine flow. Uric acid is secreted by the tubular cells of the kidney. It has a pronounced diuretic effect both in the isolated kidney and in the intact animal. In the intact animal and in heart-lung-liver-kidney preparations, injected uric acid is mainly oxidized rather than excreted. The oxidation takes place in the liver and the oxidation product is allantoin.

ARTHUR LOCKE.

HISTOCHEMICAL STUDY OF NORMAL TESTICLES AND AFTER AUTOLYSIS. F. BATTAGLIA, *Haematologica*. **7**:189, 1926.

The assumption of a trophic function of the interstitial cells of the testicle is apparently sustained by the research reported here on aseptic autolysis of testicles in dogs, rabbits, guinea-pigs and mice. The fat appears first in Leydig's cells, and the intense lipolysis here prepares it for passage into the seminiferous cells. The function of the latter includes intense lipophanerosis but there is no lipodieresis. Sertoli's cells occupy an intermediate and inconstant position in regard to these functions between the two.

MECHANISM OF DEATH FROM PERICARDIAL TAMPONING. MARIO PRATI, *Riv. di patol. sper.* **1**:149, 1926.

The duration of possible survival and the chances for effectual treatment were the principal lines followed in the research on the dogs described. The pericardium was distended with physiologic solution, or it filled up with blood as the heart was stabbed or punctured. Death occurs suddenly from a vagus reflex induced by irritation of the nerve terminals in the pericardium as it is stretched. Sudden death from this cause can be warded off by severing the vagus or depressor nerves, by cocainizing the pericardium or by preventive treatment with atropine. Then there is merely a reversible arrest of the heart function from the pressure. The revival of the animals when atropine was given suggests that when the heart is suffering from intrapericardial pressure, atropine might be used until the surgeon can relieve the pressure. This removes the danger from reflex action, leaving only the mechanical factors to contend with.

THE LACTIC ACID CONTENT OF THE BLOOD UNDER PHYSIOLOGIC AND PATHOLOGIC CONDITIONS. B. MENDEL and M. BAUCH, *Klin. Wchnschr.* **5**:1272, 1926.

The blood lactic acid values of patients with cancer are normally not excessive in spite of the demonstrated glycolytic capacity of carcinomatous tissue. This is explained by the observation that continuous venous infusion of

small amounts of lactic acid does not produce an increase in the normal blood lactic acid value, and may be due to some regulatory mechanism resident in the liver.

ARTHUR LOCKE.

THE INFLUENCE OF PHYSICAL WORK ON THE OXYGEN SATURATION AND ON THE ACTUAL REACTION OF THE ARTERIAL BLOOD IN CIRCULATORY DISEASES. H. EPPINGER, F. KISCH and H. SCHWARZ, *Klin. Wchnschr.* 5:1316, 1926.

The oxygen saturation of the arterial blood in circulatory disease is seldom abnormal during a resting state and rarely falls below normal after exertion. The hydrogen ion concentration however, is usually lowered after exertion, although it may become increased as the result of hyperpnea.

ARTHUR LOCKE.

NUTRIENT CHOLESTERIN-BLOOD CHOLESTERIN-BILE CHOLESTERIN. H. ARNDT, *Klin. Wchnschr.* 5:1372, 1926.

The blood and bile cholesterol are increased following an increase of cholesterol in the diet. All of the absorbed cholesterol does not reappear in the bile.

ARTHUR LOCKE.

BLOOD COMPOSITION AND TOTAL BLOOD QUANTITY IN MOUNTAIN DWELLERS. A. LIPPMANN, *Klin. Wchnschr.* 5:1406, 1926.

Inhabitants of high mountain districts have more blood, proportionately, than persons living near sea level. The blood corpuscle volume is greater and (at 1550 meters) the hemoglobin and erythrocyte count are increased 20 per cent. These changes are not caused by the greater solar radiation but probably compensate the lower partial pressure of oxygen in these regions.

ARTHUR LOCKE.

THE DIPHASIC ACTION OF INSULIN ON THE BLOOD PRESSURE. L. HAHN, *Klin. Wchnschr.* 5:1429, 1926.

There is a primary increase in the systolic pressure after subcutaneous injection of insulin, which in nondiabetic persons is followed by a gradual decrease to a value below the original.

ARTHUR LOCKE.

THE DIAGNOSTIC SIGNIFICANCE OF THE BLOOD SUGAR CURVES AFTER GLUCOSE BURDENING IN ULCUS PEPTICUM AND CARCINOMA. G. SCHERK, *Klin. Wchnschr.* 5:1459, 1926.

The blood sugar curves in gastric and duodenal ulcer and in benign pyloric stenosis show a fasting value, a peak after the glucose administration, and a turning back to normal which are within the physiologic limits. The curves in carcinoma, especially of the digestive tract, show a marked and characteristic retardation which may be diagnostically useful.

ARTHUR LOCKE.

THE CALCIUM AND POTASSIUM CONTENT OF THE WHOLE BLOOD IN CIRCULATORY DISEASES AND ITS BEHAVIOR UNDER PHYSICAL EXERTION. F. KISCH, *Klin. Wchnschr.* 5:1555, 1926.

The calcium and potassium content of the whole blood before and after physical exertion were studied, tabulated and correlated with albuminuria,

blood pressure, cyanosis, dyspnea and edema in fourteen patients with circulatory diseases. Without exception the calcium value was below normal when edema was present. Apparently the greater the edema, the lower the calcium. With marked insufficiency the potassium generally was considerably above normal, and occasionally normal or subnormal when insufficiency was slight. The potassium value rose following physical work in manifest circulatory insufficiency. A rise did not occur in organic heart disease, well compensated. Conclusions were not drawn.

J. D. WILLEMS.

THE RÔLE OF THE MIDBRAIN IN THE PATHOGENESIS OF ADIPOSEGENITAL DYSTROPHY. E. J. KRAUS, *Med. Klin.* **22**:485, 1926.

Kraus reports the case of a man, aged 36, who, about twenty-two months before death, suffered an injury to the head. He complained of headache and marked nervousness, developed a eunuchoid type of adiposity with pain in the fat deposits and became impotent. Postmortem examination showed a non-specific type of sclerosing encephalitis limited to the floor of the third ventricle of the brain; the hypophysis was normal except for a slight atrophy of the anterior lobe; the testicles were of normal size, spermatogenesis was present and there were few Leydig cells. Kraus is convinced that there is such a close interrelation between the hypophysis and the floor of the third ventricle that a lesion involving one will, in time, extend to the other; he believes that the obesity in this case was associated with the lesion of the brain, and the changes in the genital organs with the atrophy of the anterior lobe of the hypophysis.

J. P. SIMONDS.

THE OCCURRENCE OF NITROGEN LOSS IN FEVER. W. BIRK, *München. med. Wchnschr.* **73**:1147, 1926.

The nitrogen balance is maintained by a regulatory working together of (parasympathetic) limiting and (sympathetic) stimulative impulses on the normal tendency of the liver cells to store and resolve protein. A toxic stimulation of the cells of the protein metabolism center in the brain, as occurs in fever, produces an abnormal nitrogen balance with consequent retention or increased elimination of protein split-products.

ARTHUR LOCKE.

THE REGULATION OF BREATHING AND ITS DISTURBANCES. H. STRAUB, *München. med. Wchnschr.* **73**:1183, 1238, 1926.

This is a discussion of the mechanism by which respiration is so regulated as to assist in maintaining a constancy in the p_H and general composition of the blood.

ARTHUR LÖCKE.

THE BIOCHEMICAL EVIDENCE OF VITAL ACTIVITY OF TISSUES IN CULTURE. A. A. KRONTOWSKI, *München. med. Wchnschr.* **73**:1398, 1926.

Tissues were cultured in mediums containing known quantities of solutions of butyric, dextrose, maltose, lactose and mannite. The growth of tissue in these mediums caused a change in the p_H to the acid side, and this was taken as an index of the vital activity of the culture. By measuring this change in the hydrogen ion concentration, the activity in minute cultures could be determined accurately. Interference with the reaction by the glucose present in normal blood plasma was avoided by greatly diluting the plasma. A simpler but less accurate method consisted of adding litmus or neutral red to the medium.

J. D. WILLEMS.

Pathologic Anatomy

MYCOTIC ANEURYSM INVOLVING THE INTRAVENTRICULAR SEPTUM. CHARLES P. WILSON, *Am. Heart J.* 1:703, 1926.

Three cases of vegetative endocarditis are reported, in each of which a mycotic aneurysm involving the intraventricular septum developed. In two, the region of the bundle of His was involved in the destructive process with the development of heart block; in the third, the bundle of His escaped injury.

AUTHOR'S SUMMARY.

COR BIATRIATUM TRILOCULARE. C. ALEXANDER MCINTOSH, *Am. Heart J.* 1:735, 1926.

A case of multiple cardiac anomalies—cor biatriatum triloculare—is described which presented the following anatomic characteristics: mitral atresia, absent intraventricular septum, hypertrophied pulmonary artery becoming the descending aorta through a patent ductus arteriosus, extreme hypoplasia of the aorta, solitary (left) coronary artery, bicuspid aortic valve, accessory pulmonary vein leading from the upper portion of the right lung to the superior vena cava, anomalous communication between the left auricle and the superior vena cava.

AUTHOR'S SUMMARY.

THE PATHOLOGY OF RHEUMATIC FEVER. A CRITICAL REVIEW. BENJAMIN SACKS, *Am. Heart J.* 1:750, 1926.

The Aschoff bodies in the myocardium are periarterial collections of mononuclear and multinucleated histiocytes and constitute the specific lesions of rheumatic fever. Inflammatory foci which are almost identical are also found in the heart valves, the visceral pericardium and the aorta, and their development in these structures is probably due to the fact that their blood supply like that of the myocardium is derived from the coronary arteries; or, to put it in another way, Aschoff bodies are found near the coronary arterioles not only in the myocardium, but also in the valves, pericardium and wall of the aorta. The proliferative lesions in the periarticular tissues, the subcutaneous nodules and the brain and meninges differ superficially from the Aschoff nodules, but when allowance is made for the differences in histologic structure of these tissues, the lesions are essentially comparable to those in the heart. It is characteristic for the nodular foci to exhibit central necrosis, and frequently for the smaller vessels near them to show conspicuous alteration, with or without thrombotic occlusion. Vascular injury of a characteristic type, but without thromboses, also develops in organs in which there are no nodules. The presence of the Aschoff bodies in the heart, together with contiguous edema and possibly ischemic areas consequent on blood vessel involvement, unquestionably explains certain of the clinical cardiac phenomena; but it is difficult to account for the almost constant occurrence of the electrocardiographic changes by the presence of the anatomic lesions alone, for these are often absent or inconspicuous.

The body reacts in still another way to the infecting agent of the disease, namely, by the development of certain exudative phenomena. These are manifested by the exudation of serum into the periarticular tissues; by the exudation of serum, fibrin and cells into the synovial, pericardial and pleural cavities; and by the exudation of polymorphonuclear leukocytes in the areas near the proliferative lesions. Antirheumatic drugs cause a subsidence of the exudation

in and about the joints (which are responsible for the acute articular symptoms), but as Swift has shown, they are without effect on the periarticular proliferative lesions. It is also known that the subcutaneous nodules, Aschoff bodies in the heart and valvular disease continue to develop even if these drugs are exhibited in maximal doses.

The infecting agent probably reaches the valve by way of its intrinsic blood supply and initiates a diffuse interstitial inflammatory reaction with Aschoff bodies. The tiny firm verrucae on the line of closure do not cause embolism and are in themselves relatively unimportant. The interstitial valvulitis not only precedes the endocardial vegetations, but persists long after the latter have become cicatrized; and, being reactivated from time to time by fresh doses of the infecting agent or becoming chronic, ultimately leads to the development of chronic valvular disease, the progress of which is hastened and its extent aggravated by the great mechanical strain to which the inflamed valves are subjected. The presence of the specific lesions in the left auricle often leads to a gross lesion on the endocardial surface. It is possible that the auricular endocardium becomes a *locus minoris resistentiae*, so that if subacute bacterial endocarditis subsequently develops, the frequent extension of the vegetations along the wall of the auricle is explained.

The persistence of the subcutaneous nodules for many months in certain cases suggests that the proliferative lesions in the heart may last an equally long time. Clinical observations indicate that rheumatic carditis is frequently a chronic disease (Pichon), and although further pathologic studies are necessary, the evidence already available clearly points in this direction. The anatomic basis for chronicity is the Aschoff body or its homologues, which resemble infectious granulomas due to other causes, e. g., tuberculosis. The anhemolytic streptococcus may be cultivated from the blood of rheumatic fever in a certain percentage of cases; although it has not been proved that this organism is not the cause of the disease, convincing evidence that it constitutes the infecting agent has not been furnished, and further work must be done before the vexing problem of etiology may be considered solved.

AUTHOR'S SUMMARY.

ARACHNODACTYLIA: ASSOCIATION WITH CONGENITAL HEART DISEASE. R. K. PIPER and E. IRVINE-JONES, *Am. J. Dis. Child.* **31**:832, 1926.

Arachnodactylia, or "spider digits," is a condition first described in 1896 by Marfan. It is characterized by the striking length and slenderness of the extremities, and differentiated from the gigantism of glandular dystrophy by the almost invariable accompaniment of congenital anomalies such as cardiac defects, webbing of the fingers, dislocation of the lenses and many other conditions. Piper and Irvine-Jones give a detailed report of one case and review the literature.

SICKLE-CELL ANEMIA. HORACE B. ANDERSON, *Am. J. M. Sc.* **171**:641, 1926.

Sickle cell anemia is a comparatively new disease which it will be necessary to class with the hemolytic anemias. The most characteristic feature of the anemia is the sickling phenomenon, which is not constant. A diagnosis can be made from stained blood smears, although the progressive sickling observed in fresh blood after twenty-four hours is the most diagnostic feature. Latent cases of sickle cell anemia show a greenish discoloration of sclera and the sickling phenomenon but no other striking blood changes.

The case reported in this paper is unique in that it occurs in a negro boy born and reared in Pennsylvania, in that the color index is low, and in the fact that during the first six weeks the patient was under observation in the hospital it was not possible to demonstrate a progressive sickling of the fresh blood, and later, when the sickling phenomenon was obtained, the red cells retained their bizarre shape for seven or eight days.

AUTHOR'S SUMMARY.

DIVERTICULITIS OF THE COLON. J. ERDMANN, *Am. J. Obst. & Gynec.* **11**:609, 1926.

Although diverticulitis is usually a disease of the left lower quadrant, it may occur anywhere along the colon. It occurs most frequently in males, and in the fourth and fifth decade. Cases in children are also reported. The patients with diverticulitis are usually short and fat, and in the majority of patients on whom operation was performed by the author, the diverticula were usually in the fatty tabs or epiploic appendixes. On sectioning these near or at the base, the diverticulum is found. Diverticulitis, like inflammation of the appendix, may vary from an acute catarrhal inflammation to a gangrenous state. Fecal concretions are usually found in the pouches, which are sometimes multiple, and Erdmann conceives this to be the possible etiologic factor in the inflammation. Diverticulitis of long standing tends to form adhesions and eventually fistulas with adjacent viscera or tissues. The author's series includes one with the bladder and one into the ischiorectal fossa. The mucous membrane of the colon involved is usually normal. Proctoscopic examination is suggested as a means of differential diagnosis when the sigmoid is involved.

A. J. KORAK.

GIANT CELLS AND THEIR RELATION TO CASEATION IN TUBERCULOSIS. E. M. MEDLAR, *Am. J. Path.* **2**:291, 1926.

Giant cell formation in avian, bovine and human tuberculosis appears to be brought about in a similar manner. Giant cells are an indication of a reparative process in small areas of caseation or of simple necrosis of tissue—a reaction to a foreign body. Giant cells in tuberculosis are not true giant cells. They are bits of dead inflammatory tissue which have been more or less completely surrounded and invaded by mononuclear leukocytes, less commonly by lymphocytes and rarely by a polymorphonuclear leukocyte.

AUTHOR'S SUMMARY.

AUTOTRANSPLANTATION AND HOMEOTRANSPLANTATION OF THE THYROID GLAND IN THE RAT. LEO LOEB, *Am. J. Path.* **2**:301, 1926.

In all essential respects the laws governing autotransplantation of thyroid and parathyroid in the rat are the same as those established in the case of the guinea-pig. Connective tissue seems in both cases to be attracted by necrotic material; slight collections of lymphocytes are due to nonspecific conditions, such as accidental presence of foreign bodies. In both cases, a gradual elimination of these abnormalities takes place, and the autotransplant more and more resembles the autochthonous organ. Some differences exist between the methods of regulation which serve to eliminate the adverse conditions in the rat and guinea-pig, but these differences are due to factors of secondary importance, such as the size of the transplant.

After homeotransplantation of the thyroid and parathyroid, the same agencies of attack on the part of the host come into play in the rat as in the guinea-pig;

furthermore, the intensity of this reaction seems approximately the same in the two animals.

The intensity of the aggressive reaction depends on the relationship of host and donor. We carried out three series of transplantations in which the grade of relationship varied. In the third series in which we transplanted tissues from white rats to pure strains of hooded and cream rats, respectively, the intensity of the homeoreaction was greatest. There was a slight difference only between the two other series in both of which white rats served both as donors and hosts. The reaction was here slightly more intense in the first series, in which a distant relationship between donor and host could be excluded with greater certainty than in the second series.

In our second series in which a remote relationship between donor and host could not be excluded with the same certainty as in the other series, a maximum of destruction was observed during the fourth week after transplantation. From then on, an improvement in the condition of the transplant was observed. How far accidental relationship determines this result, how far a gradual adaptation between host and transplant is responsible for it, must be determined in further experiments.

AUTHOR'S SUMMARY.

AUTOTRANSPLANTATION AND HOMEOTRANSPLANTATION OF CARTILAGE AND BONE IN THE RAT. LEO LOEB, *Am. J. Path.* 2:315, 1926.

Three series of experiments were carried out, in which cartilage was transplanted in three groups of rats which differed from each other in the degree of relationship between donor and host in each series.

A definite correspondence was established between the degree of genetic relationship between donor and host in each series and the severity of the reactions against the transplant on the part of the host tissues, in particular of the lymphocytic infiltration and the invasion and replacement of transplanted fat tissues by fibrous tissue.

This applies to the homeoreactions of series I and II and also of series III. In the latter, in which we have to deal with a further-going genetic difference between host and transplant, we find in addition a necrosis of the bone and of the bone-producing zone of proliferating cartilage cells. Furthermore, while in series I and II the regenerative function of the perichondrium is interfered with, it is inhibited, although not entirely prevented, in series III.

The difference between series I and II on the one hand and series III on the other hand comes out also in the fat tissue of transplanted bone marrow. In series III it becomes entirely necrotic and is replaced by fibrous tissue at an early date, while in series I and II part of it may remain active for some time. In general, bone marrow is a sensitive tissue which under the influence of homeotoxins is readily injured after transplantation and does not at all or only incompletely recover after homeotransplantation. It thus seems to behave in a similar manner to unstriated muscle of uterus after transplantation.

Under conditions in which thyroid tissue is entirely destroyed by the reaction of the host tissue, cartilage remains alive to a large extent. If in these series lack of close genetic relationship causes any partial necrosis of the cartilage, it has this effect only in certain cases: even in series III the cartilage may remain well preserved.

In series I and II the homeoreaction against cartilage, instead of becoming more intense, decreases in intensity in the course of time. An adaptation takes place apparently between transplant and host.

In autotransplantation cartilage and fat tissue behave in a manner similar to normal nontransplanted tissue. In places in which the cartilage tissue is further removed from the sources of oxygen and food material, degeneration occurs in normal as well as in autotransplanted tissue, and the perichondrium may regenerate and produce cartilage.

AUTHOR'S SUMMARY.

CONGENITAL OBSTRUCTION IN OESOPHAGUS. H. C. FLOOD, *Atlantic M. J.* **29**:537, 1926.

The case belongs in the group showing defective development of the esophagus, with atresia and tracheal communication, accompanied by anomalous origin of the great vessels of the heart. The pulmonary artery, after giving off two branches, one to each lung, continued upward and a little outward, forming an arch, and then continued downward as the aorta. It had an opening for the vertebral arteries. The aorta proper emerged as a normal vessel, extended upward for a distance of 2.5 cm., where it bifurcated, forming the common carotid, right and left. Just beneath the right common carotid was a branch, forming the left subclavian. The ductus arteriosus was patulous. A small nodule in the large curvature of the stomach proved to be a piece of pancreatic tissue embedded in the wall.

ABSCESS OF THE SPINAL CORD. H. W. WOLTMAN and A. W. ADSON, *Brain* **49**:193, 1926.

To the twenty-nine cases of spinal cord abscess on record, one case in a girl, aged 11, is added. The chief symptom was spasticity and almost complete paralysis of the legs. There was no pain. Owing to the progression, the establishment of a level and the evidence of block, laminectomy of the sixth, seventh and eighth dorsal vertebrae was performed. When the cord was incised along the posterior median septum, the contents of the encapsulated abscess, about 1.5 cm. in length, escaped. No organism could be found in the pus on staining; there was no growth on blood agar, but a slight growth of staphylococci appeared in dextrose broth; inoculation of two guinea-pigs with the pus did not cause infection. The patient eventually made a complete recovery. In only one of the other twenty-nine cases on record did the patient survive.

FOREIGN BODY CYSTS SIMULATING PARASITIC CYSTS OF THE PERITONEAL CAVITY. C. G. GUTHRIE, *Bull. Johns Hopkins Hosp.* **39**:113, 1926.

At an operation for a long standing abdominal trouble with possibility of cysticerci, many small cysts (5 to 15 mm. in diameter), glistening white and opaque, were found on the intestines and mesentery, each containing several vegetable seeds. According to the history, these were from raspberry jam and canned tomatoes which the patient remembered he had eaten before a severe attack of abdominal pain, with nausea, vomiting, dyspnea and collapse, about three years before. Evidently there had been a perforation of an ulcer at that time.

To test the power of germination of viable seeds within the peritoneal cavity (in answer to the suggestions of this observation and the Baron Münchhausen story of the stag and the cherry stones), fresh, easily germinating tomato seeds were introduced into the peritoneal cavity of a rabbit. Several weeks later they were found, not germinated, enmeshed in fibrin in groups of six or seven. Botanists say germination is prevented by the lack of available oxygen.

E. B. PERRY.

OSTEOMYELITIS VARIOLOSA: REPORT OF A CASE OBSERVED DURING THE ACUTE STAGE. E. J. HUENEKENS and LEO G. RIGLER, J. A. M. A. 87:295, 1926.

In a case of nonsuppurative osteomyelitis variolosa, observed during the acute stage, destructive lesions about the epiphyseal lines of all the long bones and in the body of the first cervical vertebra were observed in a child, appearing almost simultaneously with the eruption of the variola.

Dislocation of the first cervical vertebra occurred. Eleven months later, there was practically complete repair of all the lesions. An abnormally early closure of the epiphyseal line in both tibias appeared to be taking place, which explains the manner of production of the bone deformities reported by other observers.

AUTHORS' SUMMARY.

THE FUNDAMENTAL PROPERTIES OF THE FIBROBLAST AND THE MACROPHAGE. ALEXIS CARREL and ALBERT H. EBELING, J. Exper. Med. 44:285, 1926.

Monocytes and tissue macrophages become identical in appearance when they live under identical conditions. Macrophages cultivated in nutrient and nonnutrient mediums acquire different structures. Monocytes and tissue macrophages are mere functional variations of a single type. The structure of the segregation apparatus and of the mitochondria of monocytes and macrophages depends on the composition of the pericellular fluid and on the metabolic state of the cells. The monocyte and the macrophage are endowed with a number of physiologic properties which become apparent when they grow in pure cultures. The knowledge of these fundamental characteristics explains the behavior of the cells within the organism.

AUTHORS' SUMMARY.

THE PATHOLOGY OF PLEURAL ADHESIONS IN PULMONARY TUBERCULOSIS. S. R. GLOYNE, Tubercle 7:424, 1926.

In a series of necropsies the frequency of adhesions as to localization was as follows: upper lobe, interlobar fissure, pericardium, lower lobe, diaphragm, mediastinal pleura. The stages in the formation were as follows: exudation with endothelial proliferation, formation of fibrin, production of granulation tissue, formation of new capillaries, connective tissue formation. It was found that the presence of tubercle bacilli (chiefly in the granulation tissue), giant cells and caseation were characteristic of tuberculous lesions. Elastic fibers, apparently derived from the subpleural elastica, were not constant in occurrence. Pleural adhesions produced in guinea-pigs by intrapleural injections of tubercle bacilli showed essentially the same development.

MAX PINNER.

MYELOID HETEROTOPIA IN SAPONIN POISONING. A. FABRIS, Haematologica 7: 229, 1926.

The property of inducing aberrant proliferation of bone marrow possessed by saponin was utilized by Fabris for research on the origin and evolution of megalokaryocytes. Clumping of several megalokaryoblasts may result in formation of a megalokaryocyte, or the latter may develop by growth and incomplete gemmations from a single primary nucleus. The author will report later on the behavior of the reticulo-epithelial system in saponin anemia.

A SPECIAL HEMATOLOGIC FEATURE OF ENDOCARDITIS LENTA AND KINDRED FEATURES IN VARIOUS OTHER CONDITIONS. L. FONTANA, *HAEMATOLOGICA* 7: 271, 1926.

Five colored plates show the peculiar endothelioid cells, with indications of phagocytosis, and lymphocytoid cells found in the blood dropping from a puncture of the ear after rubbing it, in 39 per cent of eighteen cases of subacute endocarditis. Nothing like this was evident in twelve normal persons and in ninety-eight persons with other diseases. The presence of these peculiar cells or bodies resembling blood platelets suggests that the endothelium of the vessels may share in the production of blood platelets—like the megalokaryocytes—besides having a phagocytic function. The elements of the walls of the small vessels thus possess a polymorphism beyond what hitherto has been assumed and a more direct share in the formation of the cells of the blood stream.

MODIFICATION OF THE PHAGOCYTIC PROCESS AND OF THE STAINING PROPERTIES AFTER SPLENECTOMY. A. LUZZATTO, *Haematologica* 7:383, 1926.

In splenectomized guinea-pigs, the cells of the lymph glands after incorporation of erythrocytes, homogenize the latter and become strongly acidophil. Luzzatto calls this the "funzione emocateretica."

GENESIS OF FETAL INCLUSIONS. M. BUDDE, *Beitr. z. path. Anat. u. z. allg. Pathol.* 75:357, 1926.

Budde describes a retroperitoneal teratoid mass in a boy, aged 2 months. There were rudimentary limb buds, but the bulk of the mass was made up of histoid derivatives of the three germ layers. He summarizes ten other examples of abdominal teratoid tumor for which he accepts a retroperitoneal situation. A discussion of the possibilities which may lead to such so-called fetal inclusions leads him to accept the monogerminal origin, as developed by Schwalbe, in preference to a bigerminal origin, as postulated by Lexer. Division of an original single embryo may lead to a complete series which would have at one extreme two equal normal twins and at the other extreme an included formless teratoid mass, with, as intermediate forms, the various double monstrosities. The degree of maldevelopment depends on the period in embryogenesis at which the embryoschisis occurs. If this happens at a time up to the end of gastrulation, a double monster results, the less completely developed portion being attached externally to the host. If the separation occurs during the stage of the formation of the primitive streak, then one portion is included within the other, the inclusion manifesting itself as a teratoid mass situated anywhere within the host.

O. T. SCHULTZ.

LATE CHANGES IN OLD TUBERCULOUS LESIONS. H. WURM, *Beitr. z. path. Anat. u. z. allg. Pathol.* 75:398, 1926.

In old tuberculous foci, Wurm describes the ingrowth of nonspecific granulation tissue into the fibrous capsule of the tuberculous area. This process is considered one of organization and leads to the complete or partial removal of the calcium-rich necrotic material. Bone formation in such old lesions is a secondary process, which occurs in the ingrowing granulation tissue as the result of the overloading of this tissue with calcium salts.

O. T. SCHULTZ.

HETEROTOPIC ENDOMETRIAL GROWTHS. K. WALZ, *Centralbl. f. allg. Path. u. path. Anat.* **37**:290, 1926.

In eight operative specimens the growths occurred in navel tumors twice, in laparotomy scars three times, in the right groin and on the cecum once each and once in Douglas culdesac, accompanied by a decidual reaction in a four months gravida. In the latter place they were also encountered in a puerpera at autopsy. In each instance participation in menstruation was demonstrable by a history of pain and swelling at the periods or by the presence of hemosiderin microscopically. Walz reviews the theories of Halban, Meyer, Sampson and Louche on this subject, agrees with the latter in many respects and advances the following theory: Bipotent coelomic epithelial basal cells give rise to unipotent cells with either endometrial or serosal potentialities, and from these specialized nonproliferative endometrial or serosa cells are formed. Bipotent cells scattered in the serosa may thus give rise to endometrium.

GEORGE RUKSTINAT.

OBSERVATIONS ON THE ETIOLOGY OF PERICARDIAL DIVERTICULI. W. GRABOWSKI, *Centralbl. f. allg. Path. u. path. Anat.* **37**:388, 1926.

In a woman, aged 50, dying from syphilitic aortitis and mitral insufficiency, a pericardial diverticulum 3.8 by 2.2 by 2 cm. was found on the right side in front, four finger-breadths from the pericardio-epicardial transition. It connected with the pericardial sac by a patent stalk and contained serous fluid. Microscopic examination revealed a cuboidal epithelial lining for the cyst, blood distended vessels surrounded by lymphoid and plasma cells and a few leukocytes in the fibrous membrane, and a circumscribed plasma and lymphoid cell collection near the lumen, surrounded by free blood and a zone of hemosiderin-containing cells. According to the classification on a traction, pulsion or congenital basis, the case reported belongs to the pulsion type occasioned by a localized weakening of the pericardium.

GEORGE RUKSTINAT.

OBSERVATIONS ON PERIRENAL HYGROMA. T. FAHR, *Centralbl. f. allg. Path. u. path. Anat.* **37**:433, 1926.

Fahr defines this condition as one in which the kidney capsule is separated from the kidney by a cavity lined with connective tissue, not connected with the kidney pelvis and filled with fluid devoid of urinary constituents. These conditions were fulfilled in a tumor the size of a child's head found in a man 73 years old. There was a blood-stained nodule in one part of the capsule. Fahr thinks the underlying process is akin to pachymeningitis hemorrhagica and that the hematoma may liquefy and form cysts or become transformed into fibrous connective tissue. The suggested etiology as nephritis, nephrolithiasis and hydronephrosis, he regards as of too frequent occurrence to serve as a starting point for the perirenal hygroma. Subcapsular lymph stasis as observed by Minkowski may be a factor.

GEORGE RUKSTINAT.

ORIGIN OF GASTRIC AND DUODENAL ULCER. H. PUHL, *Virchows Arch. f. path. Anat.* **260**:1, 1926.

On the basis of a microscopic study of the tissue obtained in 140 subtotal gastrectomies performed for gastric or duodenal ulcer, Puhl devotes 109 pages to a description of his observations and to the discussion of the origin of ulcer. He believes that two distinct problems are involved in the origin of

ulcer and in the chronicity or nonhealing of ulcer. It is with the former of these two problems that Puhl concerned himself, directing his attention to the mucosa rather than to the ulcer itself. In 27 per cent of his 140 specimens an erosive or ulcerative gastritis or duodenitis was present. The diffuse inflammatory process was characterized by catarrhal desquamation of the epithelium between the mouths of the glands, focal infiltration of leukocytes or lymphocytes, edema and, finally, erosion and superficial ulceration. The ulcerative process may make its way through the muscularis mucosae and into the submucosa. Puhl emphasizes the great frequency of the diffuse inflammatory involvement of the gastric and duodenal mucosa and the almost universal tendency of the process to heal and to recur. He believes the results of the process are chronic gastritis in most persons, going on to atrophy of the mucosa if the inflammatory process and its healing recur often enough, and chronic ulcer in others. The chronic ulcer develops from an acute ulcer, but only in certain definite regions as the result of functional mechanical factors. The results of the bacteriologic examination of the acutely inflamed mucosa were such as to lead him to conclude that the process is not bacterial but chemical in origin. Of chemical agents he ascribes little importance to the gastric juice, maintaining that lesions of the mucosa tend to heal spontaneously in the presence of gastric juice. More important are substances introduced with the food, such as alcohol, sodium chloride, etc., to which the gastric mucosa of one person may be more susceptible than that of another. Coming out strongly in favor of the inflammatory origin of gastric and duodenal ulcer, Puhl attaches little importance to the other factors usually considered important, namely, bacterial infection, peptic activity, acid necrosis, or localized vascular spasm or occlusion.

O. T. SCHULTZ.

HEMOCHROMATOSIS. HELENE HERZENBERG, *Virchows Arch. f. path. Anat.* **260**:110, 1926.

The author reports three cases of hemochromatosis. She concludes that the disease is a definite entity, consisting primarily of a disturbance of iron metabolism. The pathogenic sequence of symptoms is pigmentation, cirrhosis of the liver and diabetes.

O. T. SCHULTZ.

OCHRONOSIS. L. PUHR, *Virchows Arch. path. f. Anat.* **260**:130, 1926.

Puhr reports a case of ochronosis in a woman, aged 59, with osteomalacia, who died of cardiac decompensation due to arteriosclerosis. The pigment present in the various cartilages did not give the reactions of hematin, melanin or lipochrome.

O. T. SCHULTZ.

VASCULAR CHANGES IN CASEOUS TUBERCULOUS PNEUMONIA. T. KONSCHegg, *Virchows Arch. f. path. Anat.* **260**:140, 1926.

As the most striking change in the vessels of the lung in caseous tuberculous pneumonia, Korschegg describes proliferation of the connective tissue of the adventitia, the newly formed tissue being infiltrated by lymphocytes and plasma cells. The intima is thickened to a varying degree by young tissue. The latter comes from the adventitia, penetrates the wall of the vessel, and spreads out beneath the endothelium. The inflamed vessel wall may undergo caseation necrosis before the lumen is obliterated. The author believes that it is possible

to determine from the degree of proliferative reaction of the vessels the degree of resistance which the patient had, opposed to the tuberculous process.

O. T. SCHULTZ.

HEMATOPOIESIS IN RECURRENT FEVER. OLGA BYKOWA, *Virchows Arch. f. path. Anat.* **260**:169, 1926.

Active hematopoiesis with the formation of both erythrocytes and granulocytes is described in the bone marrow, spleen, lymph nodes and suprarenal. The cells of the reticulo-endothelial system are stimulated to hypertrophy and proliferation, and become markedly phagocytic. Necroses were present in the bone marrow, spleen and lymph nodes.

O. T. SCHULTZ.

RETICULO-ENDOTHELIAL HYPERPLASIA. R. AKIBA, *Virchows Arch. f. path. Anat.* **260**:262, 1926.

A girl, aged 10 years, died in the fifth week after the development of acute ulcerative tonsillitis, the clinical course having been that of a septic infection with purpura. The lymphoid tissue of the spleen, lymph nodes, tonsils and intestinal follicles was to a great extent replaced by large epithelioid cells which were separated by a fine reticulum and which were believed by Akiba to be proliferated cells of the reticulo-endothelial system. Since the latter system is held by some to have hematopoietic properties, Akiba discusses the possible relationship of his case to acute leukemia. He concludes that there is no relationship and that his case was one of sepsis with proliferation of reticulo-endothelial cells, which manifested no hematopoietic properties.

O. T. SCHULTZ.

FORMATION OF TUBERCULOUS GIANT CELLS. G. BAKÁCS, *Virchows Arch. f. path. Anat.* **260**:271, 1926.

In four of one hundred cases of tuberculosis, eighty of which were active and twenty healed, Bakács found giant cells with multiple, centrally situated nuclei. His interpretation of the formation of the typical Langhans giant cell with its peripheral nuclei, in the light of the cells with central nuclei seen by him, is hypertrophy of an endothelioid cell at the center of the tubercle as the result of the action of the toxin, amitotic nuclear division without cell division, and central necrosis of the cell body and of some of the centrally located nuclei, the rest of the nuclei being pushed to the periphery of the cell. He concludes that the presence of giant cells in tuberculosis is evidence of the progressive character of the process; their absence indicates cessation and healing of the process.

O. T. SCHULTZ.

LOCALIZATION OF MILIARY TUBERCLES IN THE SPLEEN. E. GRABERG, *Virchows Arch. f. path. Anat.* **260**:287, 1926.

By means of serial section and reconstructions, Graberg established that the primary localization of miliary tubercles in the spleen is along the arterioles of the malpighian bodies. Those present in the red pulp, trabeculae or capsule are secondary to the malpighian body tubercles.

O. T. SCHULTZ.

SYNDACTYLIA WITH LOCALIZED LIPOMATOSIS. H. FERIZ, *Virchows Arch. f. path. Anat.* **260**:308, 1926.

Feriz reports two cases of unilateral syndactylia of the foot with localized lipomatosis. For the condition discussed he proposes the name *macro dystrophia lipomatosa progressiva*, and thinks it is to be differentiated from localized gigantism with syndactylism, that is, *macro dactylia simplex congenita*. The former he defines as a progressive tumor-like increase of adipose tissue, which develops in postfetal life on the basis of a congenital syndactylism and is associated with hypertrophic and dystrophic changes in the syndactylic bones. The lipomatous overgrowth is not heritable, although the syndactylia is. The cause of the adipose overgrowth, like that of the digital deformity, is unknown, but Feriz does not think that the former is a developmental anomaly. With the statement that he makes no claim for completeness, he tabulates 187 cases of partial gigantism which show all stages from simple hypertrophy of all the tissues to the dystrophic lipomatous condition described by himself. From this tabulation he selects nineteen cases which correspond to his own. A bibliography of 332 references is appended.

O. T. SCHULTZ.

REGENERATION IN THE SPINAL CORD. N. SSAMARIN, *Virchows Arch. f. path. Anat.* **260**:369, 1926.

Ssamarin studied regeneration of the spinal cord of rabbits after making a longitudinal incision under aseptic precautions. No regeneration occurred in the gray matter. In the white matter regeneration occurred in two stages. During the first stage, which was complete in two months, new axis cylinders were formed, and then degenerated and were resorbed. Beginning with the third month, new axis cylinders were again formed. These persisted and grew through the scar, but the process was held to have no clinical significance because the axis cylinders found no proper paths for growth, and their regeneration was, therefore, a useless phenomenon.

O. T. SCHULTZ.

GOITER IN HENS. E. FRITSCHI, *Virchows Arch. f. path. Anat.* **260**:422, 1926.

Thyroid enlargement is said to be rare in birds. Two examples of goitrous enlargement of the thyroid of the hen are recorded; one is termed a diffuse adenomatous and vascular struma, the other a diffuse proliferating parenchymatous struma. It is of some interest that the report comes from Zürich.

O. T. SCHULTZ.

CIRCUMSCRIBED TRAUMATIC OSSIFYING MYOSITIS. K. VON DITTRICH, *Virchows Arch. f. path. Anat.* **260**:436, 1926.

Circumscribed ossifying myositis is classified as traumatic, nontraumatic and neurotic. Von Dittrich's discussion relates to the first named of these three varieties. The two theories of the pathogenesis of the condition, that of periosteal misplacement and that of metaplasia, are reviewed, the author concluding that there is little evidence in favor of the view that circumscribed ossifying myositis is due to the traumatic misplacement of bits of periosteum which manifest osteogenetic properties in their new situation. In two cases studied histologically by von Dittrich the area of injured muscle was replaced by cellular, young mesenchymal tissue in which were islands of cartilage. The latter was in process of transformation to bone. He concludes, therefore, that

the ossification occurs by indirect metaplasia, that is, by the formation of a dedifferentiated supporting tissue which differentiates into cartilage and bone. Attempts to reproduce the condition experimentally by traumatizing the muscles of guinea-pigs, kept on alternating acid and alkaline diets with high calcium content, were unsuccessful. Marked calcification resulted, but there was no true bone formation. The author thinks that too high a calcium content of the blood and tissues may interfere with the bone forming potentialities of the dedifferentiated stroma.

O. T. SCHULTZ.

HETEROTOPIC BONE FORMATION. G. B. GRUBER, *Virchows Arch. f. path. Anat.* **260**:457, 1926.

The paper by von Dittrich led Gruber, who has devoted much attention to ossifying myositis, to present a general discussion on heterotopic bone formation. He denies that the periosteum has osteogenetic properties and that misplacement of fragments of periosteum can have anything to do with extraskeletal ossification. On the other hand, he deprecates the use of the term metaplasia, when this is used to connote the transformation of fibrous tissue into bone or its replacement by bone. Heterotopic bone formation occurs in an undifferentiated mesenchymal matrix which has the potentiality of differentiating in several directions.

O. T. SCHULTZ.

ARTHRITIS DEFORMANS. J. HEINE, *Virchows Arch. path. Anat.* **260**:521, 1926.

This 143 page monograph, with one of 193 pages by Schürmann, makes up a complete number of *Virchow's Archiv für pathologische Anatomie und Physiologie und für klinische Medizin* dedicated to Schmorl on his sixty-fifth birthday. In discussion of what is meant by arthritis deformans, Heine says that if he were asked to define what he understands by the term he would disregard histogenetic considerations and would limit himself to etiologic and pathogenic ones. Arthritis deformans he considers a group name applied to the effects of a variety of factors which may act on joints. This introduction is followed by a detailed microscopic description of the noninflammatory lesions of joints, with special attention to the cartilage and the subchondral tissue. This study emphasizes the gradual transition from minor changes to those of well marked arthritis deformans. He then analyzes his material, derived from 1,002 necropsies, according to age, sex, the individual joints involved and the process present. This section is followed by one devoted to the theories of the etiology and pathogenesis of arthritis deformans. He concludes that a variety of factors, many of which are still dark, are concerned, most important among which are heredity, constitution and disposition, which manifest themselves in differences of the structure and composition of the body tissues and fluids of the individual. Functional and mechanical factors are only of secondary importance.

O. T. SCHULTZ.

ACUTE LEUKEMIA. KWASNIEWSKY and N. HENNING, *Ztschr. f. klin. Med.* **103**: 189, 1926.

The chronic leukemias can usually be distinguished hematologically, as well as histologically, in two known varieties—lymphatic or myelogenous. Difficulties in differentiation arise, however, in instances of leukemia which run an acute course. Moreover, it is commonly believed that in instances their

separation in two groups is impossible. Kwasniewsky and Henning produce evidence to show that every case of acute leukemia possesses individual peculiarities. The two kinds of leukemia can be differentiated, however, by a careful hematologic and histologic examination. This report concerns itself with four new cases of acute leukemia examined clinically and post mortem.

From twenty-seven cases (twenty-three previously reported) studied, the authors arrive at the following conclusions:

1. Histologically all the cases showed a definite separation into two groups, according to the theory advocated by the "dualists."

2. The differentiation between myeloblasts and lymphoblasts in atypical cases is possible tinctorially as well as morphologically.

3. The monocytes furnish partly a positive oxydase reaction. It is, therefore, questionable whether this reaction, particularly when it is not outstanding, is peculiar to cells of the myeloid variety only.

4. The arrest of the overaccelerated leukopoiesis following the application of roentgen rays to the spleen indicates that it concerns here a mobilization of ferments which act on the mesenchyme interfering with the new formation of leukocytes.

B. M. FRIED.

AN EXPERIMENTAL STUDY OF THE HISTOGENESIS OF EXTRAMEDULLARY MYELOPOESIS. F. J. LANG, *Ztschr. f. mikr.-anat. Forsch.* 4:417, 1926.

Rabbits were subjected to a series of carmine injections, followed by the injection of irritants such as colon vaccine, colon bacilli and sapotoxin. Extramedullary myelopoiesis was observed in the liver, suprarenals, omentum and particularly the lymph glands. In the three former organs its beginning was in most cases intravascular, in the venous capillaries and small veins. Circulating hemocytoblasts aggregated in the lumen, hypertrophied and underwent mitotic division, and developed into eosinophilic and special myelocytes. When there was a well-defined endothelial lining, the process remained restricted to the lumen for a long time, tissue invasion taking place only as a late stage. Where the vascular boundary consisted of histiocytes (liver, suprarenal), the invasion occurred early. The most noteworthy fact was the undifferentiated character of the early hemocytoblastic colonization.

In the suprarenals was also observed the development of foci of myeloid cells in the outer portions of the walls of the larger medullary veins, with eventual escape of the developing cells inward into the lumen. This the author interprets as the evolution into myeloid tissue of undifferentiated mesenchyme, although he recognizes the possibility of the foci representing aggregations of cells which had wandered out from the lumen.

In the lymphoid organs, spleen and lymph glands, both types of myelopoiesis were observed, with the second type in predominance. Here the outstanding phenomenon was the development of myeloid cells in the lymph follicles, especially in the germ centers, from the basophilic cells, the hemocytoblasts or "large lymphocytes." In addition, in certain circumstances, hemocytoblasts could be seen developing from undifferentiated reticular cells.

From the foregoing, the author deduces the existence of a common, undifferentiated blood-forming tissue, formed of hemocytoblasts. These cells may reach an organ, the site of extramedullary myelopoiesis, through the blood stream, or they may originate locally, as in the embryo, through the development of undifferentiated cells.

H. E. EGGERS.

ZUR KENNTNIS DER PNEUMATOSIS CYSTOIDES INTESTINORUM. JOHN NAESLUND, Path anat. und exper. Stud. 1924. Stockholm: Isaac Marcus Boktryckeriaktiehlag.

Besides a thorough review of the history and literature concerning gas cysts of unknown etiology in the intestinal wall, the mesentery or nearby structures, details are given of the pathologic anatomy of nine cases in swine, and of three cases (including clinical notes) in man. In old cases the cysts were most often in the wall of the small intestine, were more or less completely lined with endothelium, sometimes with swollen cells, and were occasionally partly filled with blood or coagulated lymph; and in the surrounding tissue were capillaries with thickened walls, round cells, plasma cells and leukocytes, often eosinophils.

From the walls of the cysts in hogs were isolated several strains of gram-negative, gas-producing, rods, evidently of the coli group, which were named *Bacterium pneumatosus*. These bacteria, or their extracts, gave positive immune reactions (agglutinin, opsonin, precipitin and especially complement fixation) with serums from hogs with cysts, and from rabbits immunized with these organisms, but not with serum from unaffected hogs. Tissue reactions to injections of these bacteria were similar to those described in the tissue about the spontaneous cysts, and also to those produced by injections of this cystic tissue after which the pneumatose bacterium could be isolated in nearly pure culture.

The gas, from cysts not exposed to air and opened under water, contained oxygen from 0.5 to 1.4 per cent (increased to 20 per cent in cysts exposed to air), and carbon dioxide from 0.3 to 1.4 per cent; nitrogen makes up most of the remaining volume. The gas produced by the pneumatose bacterium in four day, 3 per cent swine liver broth cultures contained nearly the same proportions, oxygen, from 0.8 to 1.7 per cent, and carbon dioxide from 1.4 to 2.1 per cent, and so strengthened the suggestion that the bacteria found in the walls of the cysts may be there during the life of the animal and be a causative factor in the formation of the cysts.

ETHEL B. PERRY.

Pathologic Chemistry

BLOOD SUGAR IN STATUS THYMICOLYMPHATICUS. AUBREY B. MACLEAN and RUTH C. SULLIVAN, Am. J. M. Sc. 171:659, 1926.

In three cases of status thymicolymphaticus the blood sugar values were low (42, 52, 57 mg. per hundred cubic centimeters). In one case of suprarenal hemorrhage a blood sugar of 25 mg. per hundred cubic centimeters was found. In six cases of convulsions produced by conditions other than status thymicolymphaticus the blood sugar contents were normal or increased above normal. In six cases of enlarged thymus shown by roentgenograms, the blood sugar was within normal limits in five and slightly decreased in one. In six cases in which the blood sugar was determined within half an hour before death on patients with diseases other than status thymicolymphaticus, the values were normal or above normal.

Acute suprarenal insufficiency is suggested as the immediate cause of sudden death in status thymicolymphaticus.

AUTHORS' SUMMARY.

THE GLUTATHIONE CONTENT OF ANIMAL TISSUES WITH REFERENCE TO TUBERCULOSIS. NAO UYEI, *J. Infect. Dis.* **39**:73, 1926.

The glutathione content of the various organs in some of the common experimental animals, rat, guinea-pig, rabbit and dog, reveals a constancy in the amount in each organ of the individual species and a characteristic constant amount for each of the different species. The glutathione occurs in the order of decreasing amounts in the lens, liver, spleen, kidney, suprarenals, testicles, lung, brain, marrow, heart and muscle. This order is in exact agreement with that given by Salkowski and Yamagiwa for the oxidizing power of certain animal tissues toward salicylaldehyde. Blood serum contains no glutathione while the corpuscles reveal a small determinable amount.

No relation exists of the species tested to tuberculosis, between the glutathione content of the various organ tissues and the organ susceptibility.

The glutathione content of animal organs remains constant during fasting, probably because of the stability of this compound in the animal body as well as in vitro in distinction to the instability and variability of catalase.

AUTHORS' SUMMARY.

THE FUNCTION OF A PHOSPHATASE IN BONE-FORMATION. H. D. KAY, *Brit. J. Exper. Path.* **7**:180, 1926.

In normal blood-plasma a small quantity of an acid-soluble phosphoric ester is present which is hydrolyzable by bone phosphatase. This may be an important factor in bone-formation and maintenance. The phosphatase content of the whole bone is extremely high in fetal life, but diminishes as the rate of bone-formation decreases. In the whole kidney, the phosphatase is lowest in the fetal stage, and rapidly increases as the kidney becomes functional.

S. A. LEVINSON.

CONCRETION FORMATION FROM THE COLLOID-CHEMICAL POINT OF VIEW. M. ADOLF, *Klin. Wchnschr.* **5**:1257, 1926.

This is a review of the many attempts to clarify the nature of the origin, growth and shaping of concretions on the basis of colloid chemical relations.

ARTHUR LOCKE.

VARIATIONS IN THE CELLULAR AND CHEMICAL COMPOSITION OF THE BLOOD DURING PREGNANCY. G. H. SCHNEIDER, *Klin. Wchnschr.* **5**:1422, 1926.

This is a review. During pregnancy, the composition of the blood varies between normal values and those characteristic of toxemia.

ARTHUR LOCKE.

THE RECOGNITION OF PEROXIDASES IN SERUM. S. KWASNIEWSKI and N. HENNING, *Klin. Wchnschr.* **5**:1472, 1926.

The concentration of peroxidase in the plasma may be an index of the amount of leukocyte disintegration. Traces of peroxidase are found in normal serum in leukocytosis and in lymphatic leukemia. They are absent in myeloic leukemia.

ARTHUR LOCKE.

BLOOD LACTIC ACID AND CARCINOMA. H. E. BÜTTNER, *Klin. Wehnschr.* **5**:1507, 1926.

The blood lactic acid is not normally increased in carcinoma except when there are complications such as anemia, obstruction and fatty degeneration (especially of the liver).

ARTHUR LOCKE.

FURTHER HEART-HORMONE RESEARCHES. L. HABERLANDT, *Klin. Wehnschr.* **5**:1522, 1926.

A substance resembling but not identical with epinephrine may be extracted from heart muscle with alcohol. It is insoluble in ether, difficultly soluble in chloroform, thermostable and dialyzable.

ARTHUR LOCKE.

THE OCCURRENCE OF HIGH VALUES OF THE BOUND AND FREE AMINO NITROGEN IN DEPROTEINIZED BLOOD IN LEUKEMIA. E. BECHER and E. HERMANN, *München. med. Wehnschr.* **73**:1312, 1926. INVESTIGATIONS OVER THE RELATIONS BETWEEN THE VALUE OF THE FREE AND BOUND BLOOD AMINO NITROGEN WITH THE NUCLEATED CELL CONTENT OF THE BLOOD; A CONTRIBUTION TO THE KNOWLEDGE OF THE BLOOD AMINO NITROGEN IN DIFFERENT ANIMAL SPECIES. *Ibid.*, p. 1230.

The increased blood amino nitrogen values observed in patients with leukemia who have high leukocyte counts are due entirely to an increase in the amino nitrogen contributed by the leukocytes.

Animals with nucleated red cells have higher normal blood amino nitrogen values than mammals.

ARTHUR LOCKE.

Microbiology and Parasitology

DENGUE, ITS HISTORY, EPIDEMIOLOGY, MECHANISM OF TRANSMISSION, ETIOLOGY, CLINICAL MANIFESTATIONS, IMMUNITY, AND PREVENTION. J. F. SILER, MILTON W. HALL and A. PARKER HITCHENS, Manila, Bureau of Printing, 1926.

At the time of the Spanish-American war yellow fever was prominent in the thoughts of medical men living or visiting tropical countries where this disease was endemic, and certain persons (Finlay) had accumulated sufficient evidence to incriminate the mosquito as a probable transmitter. The urgent need of finding an answer to the yellow fever problem because the United States Army of occupation in Cuba consisted practically entirely of nonimmunes resulted in that final and successful effort of Walter Reed and his co-workers.

Dengue, a disease symptomatically not unlike mild cases of yellow fever, has been studied now and again by various research men, and gradually opinion has been crystalizing in such a way as to reveal rather clearly that mosquitoes are responsible, and incriminating evidence has been furnished against two species. Recent outbreaks in the southern part of the United States, researches accompanying these and similar investigations elsewhere had practically incriminated *Aedes aegypti*. Cleland, Bradley and McDonald's work was practically final proof of the transmission by *Aedes aegypti*.

The investigation of this disease was planned as one of the major problems of the United States Army Medical Department Research Board on its establishment in 1922, as the successor of the board for the study of tropical disease existant in the Philippines up to the year 1913.

How successful was the attack on this condition is revealed in the monograph by Siler, Hall and Hitchens, published by the Philippine Bureau of Science. The book comprises approximately five hundred pages and deals with every phase of dengue in the first half. The rest contains a reference list and an appendix showing the details of each individual experiment, with photographs illustrating the technic under which the work was done. It should be consulted in the original by those interested.

The history of the disease is traced with considerable certainty back to the early seventeenth century, and it appears probable that the condition, characteristically endemic, was present on this continent at the time of its discovery. The various reports of experiments in mosquito transmission of the disease are given and discussed critically. Some results obtained in previous research are difficult to harmonize with the work of this board (Ashburn and Craig; Chandler and Rice). It is quite possible that some of the reported infections were by mechanical transmission of the virus, a theoretical possibility, as is indicated by the successful production of the disease with blood filtrate, as originally reported by Ashburn and Craig.

As the result of this investigation there are now answers to practically all of the questions with reference to the disease, with the exception of the character of the etiologic agent. A great deal of effort was made by this board to discover this agent, and many of the pitfalls which in the past have led to the "discovery" of parasites believed to be etiologically responsible were exposed. Since the demonstration of a member of the spirochete group in patients suffering with yellow fever, known to be transmitted by the *Aedes aegypti*, and knowing that the parasites of these diseases both required a similar length of stay in the body of the mosquito before the latter could transmit infection, research workers have enthusiastically hunted for a spirochete in patients with dengue. From what little knowledge is possessed of the biology of the spirochete group, it would seem rather more reasonable to expect a transmission directly rather than following a life cycle, in an insect which, so far as is known, is not required by any of the known members of the spirochete group; and, with the exception of the relapsing fever, organisms are not transmitted, at least usually, by insects. Yellow fever, dengue and pappataci fever are quite similar and resemble diseases due to animal parasites, the possible exception being that in at least one, yellow fever, a pronounced degree of immunity results from the attack.

The safeguards about the mosquito experiments were as near absolute as it is possible to make them; only bred mosquitoes were used, and a considerable proportion of the early period of the work was spent in determining methods of raising the different species. These methods should be consulted in the original. The utmost safeguards were thrown about the ward in which the experiments were made, which was as absolutely mosquito proof as possible. Mosquitoes were not seen in it, except in the cages used to transport them, within two months of the occurrence of the first experimental case of dengue. Only eight mosquitoes including four *Aedes aegypti* were detected in the ward during the entire nine months of the experimental period. The work was all done on volunteers—men of short residence in the tropics, who were observed a more than adequate time for the development of any infection, had it existed prior to their domicile in the ward.

The transmission experiments reported include fourteen blood inoculations, five of which were positive; 111 biting experiments with *Aedes aegypti*, forty-seven of which were positive; and seven biting experiments with *Culex quinquefasciatus*, none of which was positive. The disease developed characteristically in each case, and was usually accompanied by a rash, though the latter was

sometimes evanescent. It was found that mosquitoes were successfully infected for a short time before the actual appearance of symptoms of the disease and for the first three days of its course. The minimum time required for the development of the virus in the mosquito was eleven days, and evidence was presented to show that at this period development was less complete than later, for infections were not as successful as on the twelfth to the fourteenth days. Thereafter mosquitoes remained infectious throughout their life. One case was produced by a mosquito which had been infected seventy-five days previously.

Sixty-four volunteers were used. Six of these men were found to be immune to infection by mosquitoes known to be capable of transmitting the disease, and five also were shown to be immune to direct blood inoculation. In nine men, the requirements outlined in preceding paragraph were not met, but they were found to be susceptible by blood inoculation. In the balance of forty-nine cases all requirements were met, and forty-seven cases of dengue were produced, with approximately 96 per cent morbidity. The other two patients did not show a typical reaction and were recorded as having uncertain cases.

The epidemiology of the disease in the Philippines was studied thoroughly. It is generally distributed throughout the islands but infrequently attacks the native in recognizable form, the assumption being that this is due to an acquired immunity. Caucasians of prolonged residence in the Philippines rarely suffer from the disease.

Complete accounts of the clinical aspects of the disease are presented. Adenopathy is usually present at the onset and this was considered a valuable differential point in the diagnosis. Leukopenia was usually found. Toxic involvement of the nervous system is considered a prominent feature in the symptomatology of dengue.

While second and subsequent attacks are common, a study of immunity in this condition indicates that a considerable degree exists for a short time after any attack, and that recurrent attacks gradually become less severe. Philippine soldiers apparently were immune to injections of blood, while caucasian soldiers who were known to have had the disease were still susceptible.

The methods of prevention are obviously the same as for yellow fever, and the practical application of these is clearly set forth, including those dependent on the determinations made in this research.

G. R. CALLENDER.

MODIFYING THE COURSE OF INFECTIONS WITH BIRD MALARIA BY CHANGING THE SUGAR CONTENT OF THE BLOOD. R. W. HEGNER and MARY STUART MACDOUGALL, *Am. J. Hyg.* 6:602, 1926.

Although attempts to decrease the extent of malarial infection in birds by treatment with insulin are not decisive, they are suggestive, and an increase of the sugar content of the blood, as by dextrose feeding, seems definitely to bring about conditions favorable for the parasite and thus prolong infection so that death ensues. Further work will be reported later.

ETHEL B. PERRY.

IS THE FORMATION OF GUARNIERI BODIES AN EXCLUSIVELY MAMMALIAN RESPONSE TO INFECTION WITH THE VACCINE VIRUS? HOWARD B. ANDERVONT, *Am. J. Hyg.* 6:618, 1926.

The conclusions from this work agree with those of Kadowaki concerning the cell inclusions. Neither in the skin nor in the cornea of rabbits after inocula-

tion with the virus of epithelioma contagiosum (poultry pox virus) were any structures found that resembled either the Bollinger bodies or the Guarnieri bodies, although the Guarnieri appeared uniformly and typically after inoculation with vaccine virus.

AMEBIC COLITIS: ITS TREATMENT BY TRANS-DUODENAL MEDICATION. ALBERT F. R. ANDRESON, *Am. J. Trop. Med.* **6**:119, 1926.

The author believes that in amebic dysentery active amebas are protected from destruction by medication through the plugging of ulcers with fibrin and debris. He recommends a course of treatment by which these plugs are removed, namely, saline catharsis by means of a transduodenal tube. A solution of powdered ipecac is given through the tube immediately after the ulcers are cleaned out, thus allowing the drug to come directly in contact with the amebas. Emetine given hypodermically may supplement the treatment. Good results appear to follow this method.

E. M. HALL.

SOME OBSERVATIONS ON THE TERTIARY LESIONS OF FRAMBOESIA TROPICA OR YAWS. L. H. BITTNER, *Am. J. Trop. Med.* **6**:123, 1926.

In the conditions known respectively as rhinopharyngitis mutilans, keratoma plantare sulcatum and juxta-articular nodules, the author notes constantly the previous history of yaws. This association, with the absence of any evidence or history of syphilitic infection, the positive Wassermann reaction and a definite response to treatment with neo-arsphenamine, is the reason for considering these manifestations as tertiary lesions of yaws.

E. M. HALL.

EXPERIMENTAL RAT-BITE FEVER. MAX THEILER, *Am. J. Trop. Med.* **6**:131, 1926.

The author presents experimental evidence tending to establish *Spirochaeta morsus muris* as the etiologic factor in rat-bite fever. A spirochete closely resembling *Spirochaeta morsus muris* was demonstrated in the blood of guinea-pigs, and blood from a typical human case of the disease was injected into white mice. White mice and rats are readily infected with the spirochete but show no symptoms although they harbor the organism in the blood for a long time. Guinea-pigs inoculated with the organism develop fever, enlargement of the lymph nodes, inflammation and induration of the external genitals and loss of hair. Rabbits were infected by subcutaneous, intradermal and intratesticular injections of blood containing the spirochetes. About half of the animals showed no symptoms, but their blood was infectious for guinea-pigs after three weeks. Strong spirocheticidal properties were developed in the serum of infected rabbits.

E. M. HALL.

ETIOLOGY OF OROYA FEVER. I. CULTIVATION OF BARTONELLA BACILLIFORMIS. HIDEYO NOGUCHI and TELEMACO S. BATTISTINI, *J. Exper. Med.* **43**:851, 1926.

A pure culture of a micro-organism, resembling in morphology and pathogenic action *Bartonella bacilliformis*, has been obtained from blood taken during life from a case of Oroya fever which ended fatally. The blood taken at Lima into citrate solution and transported to New York at refrigerator temperature yielded positive cultures twenty-eight days after its withdrawal from the patient.

The strain of *Bartonella bacilliformis* thus isolated grows well on the semi-solid leptospira medium and also on slant agar containing animal blood. The initial growth is not readily recognizable to the naked eye, but the presence of the organisms can be determined by means of the dark-field microscope and by Giemsa and Gram staining methods. No growth has been obtained on the more ordinary culture media. The organism is an obligate aerobe, is gram-negative and under certain cultural conditions is motile. All the forms which have been described as occurring in human red corpuscles may be found in the cultures and, in addition, many granular and coarsely irregular forms have been encountered.

The inoculation of cultures of *Bartonella bacilliformis* into *Macacus rhesus* produces infection and gives rise to effects which differ with the mode of inoculation. The intravenous injection of the culture into young macaques induces a prolonged irregularly remittent fever. The organism can be cultivated from the blood over a long period and it has been detected within the red corpuscles of the monkeys reproducing the precise appearances observed in cases of Oroya fever in human beings.

The intradermal injection of the culture into the eyebrow of young macaques give rise to nodular formations rich in new blood vessels and showing the bacilliform organism within the endothelial cells. From the experimentally induced nodules cultures of the organism are readily recovered.

AUTHORS' SUMMARY.

A FILTER-PASSING VIRUS OBTAINED FROM *DERMACENTOR ANDERSONI*. HIDEYO NOGUCHI, J. Exper. Med. **44**:1, 1926.

An invisible, filter-passing virus, pathogenic for the guinea-pig, and capable of cultivation on special mediums for at least seven generations, has been isolated from a tick of the species *Dermacentor andersoni*. One of two monkeys (*Macacus rhesus*) inoculated became infected, and in one rabbit the result was negative.

The virus has been transmitted from infected guinea-pigs to ticks as also in one instance by tick feeding from an infected tick to a guinea-pig. The presence of the virus in the tick is more easily demonstrated by the inoculation of guinea-pigs with a suspension of the tick viscera. Continuous high fever from (104.5 to 106.5 F.) and enlargement of the spleen are the chief symptoms of the infection in guinea-pigs. After the febrile attack the guinea-pigs are not susceptible to reinoculation with the cultured virus, but are subject to infection with the virus of spotted fever, and vice versa.

AUTHOR'S SUMMARY.

THE ORGANISM ASSOCIATED WITH SPECIFIC INFECTIOUS CYSTITIS AND PHELO-NEPHRITIS OF COWS. F. S. JONES and RALPH B. LITTLE, J. Exper. Med. **44**:11, 1926.

A gram-positive diphtheroid isolated from spontaneous cases of cystitis and phelonephritis of cows on five farms has been studied. All the strains obtained were of the same general morphology. They possess similar cultural characteristics and, to a great degree, similar agglutination affinities. The organism is not pathogenic for the ordinary laboratory animals. It produces no toxin. Cows receiving intravenous injections with broth cultures failed to

develop the disease. On the other hand, small quantities of cultures introduced into the bladder by way of the urethra gave rise to a typical persistent cystitis.

There is evidence for a transmission of the disease by contact infection, as when the same person carries both normal and infected cows.

AUTHORS' SUMMARY.

A BIOLOGICAL CLASSIFICATION OF ENCAPSULATUS PNEUMOCOCCI (FRIEDLÄNDER'S BACILLUS). LOUIS A. JULIANELLE, J. Exper. Med. **44**:113, 1926.

A biologic classification has been made of thirty strains of Friedländer's bacillus. This study reveals that there exist among these strains three sharply defined and specific types and one heterogenous group. The three types are type A, fifteen strains; type B, six strains; type C, three strains and group X, six strains. The agglutination, agglutinin adsorption, protection, thread and precipitin reactions have been employed in the working out of this classification, and the types have been proved highly specific by means of each serologic test.

AUTHOR'S SUMMARY.

A STUDY OF THE INTESTINAL FLORA UNDER NORMAL AND ABNORMAL CONDITIONS. L. S. DUDGEON, J. Hyg. **25**:119, 1926.

The feces of normal and infected persons were examined for spirochetes, streptococci, staphylococci, hemolytic colon bacilli and *B. welchii*. An abnormal fecal flora is often the result of dietetic errors, intemperance, active purgation or septic infections of the mouth, respiratory and urinary tracts. It may be rendered normal by a simple diet. The use of intestinal antiseptics or of acidophilus milk is not recommended.

ARTHUR LOCKE.

THE RELATION BETWEEN THE AGE AND THE VIRULENCE OF CULTURES OF *B. AERTRYCKE* (MUTTON). G. S. WILSON, J. Hyg. **25**:142, 1926. THE PROPORTION OF VIABLE BACILLI IN AGAR CULTURES OF *B. AERTRYCKE* (MUTTON), WITH SPECIAL REFERENCE TO THE CHANGE IN SIZE OF THE ORGANISMS DURING GROWTH, AND IN THE OPACITY TO WHICH THEY GIVE RISE. Ibid., p. 150.

Four batches of 60 mice have been injected with comparable doses of *B. aertrycke* (Mutton), taken from broth or agar cultures in different phases of reproductive activity. The mortality and the average survival time of the mice after injection varied so little among the different groups as to justify the conclusion that no difference in the virulence of this organism is detectable during the first week of growth.

Working with agar cultures of a strain of *B. aertrycke* (Mutton) it was found that the number of organisms requisite to cause a given opacity was five times as great in a 26-hour as in a 4-hour culture. This difference is probably explicable by the fact that bacilli from young cultures are larger than those from old ones. Evidence is produced which suggests that the opacity method gives a measure not of the number of organisms, but of the total quantity of bacterial protoplasm in the suspension. . . . The maximum proportion of living bacilli is reached at the end of the logarithmic phase of growth, when about 80 per cent of the organisms are alive and capable of reproduction. It seems probable that there is a mortality among the bacilli that are generated in the early stages of growth, the least resistant organisms failing to divide.

AUTHOR'S SUMMARY.

STUDIES UPON BACTERIAL SPORES. 2. INCREASING RESISTANCE TO HEAT THROUGH SELECTION. C. A. MAGOON, J. Infect. Dis. **38**:429, 1926.

Evidence is presented which shows that some bacterial spores derived from the resistant survivors in thermal death time tests possess higher resistance to heat than the original spores; and that by a process of selection a strain of bacteria may be obtained the spores of which attain a resistance at least twenty-five times that of the original spores.

AUTHOR'S SUMMARY.

THE BACTERICIDAL ACTION OF ACRIDINE DYES AND THE ADJUVANT EFFECT OF SERUM. ARNOLD H. EGGERTH, J. Infect. Dis. **38**:440, 1926.

The germicidal titer of acriflavine is markedly influenced by the nature of the medium in which the tests are made. Meat infusion, in particular, lowers the titer.

The action of acriflavine is not altered by the presence or absence of sodium or potassium salts, or of phosphates.

The acriflavine titer is very different at different hydrogen ion concentrations. Alkaline reactions greatly increase the germicidal action.

The adjuvant action of serum is due to its alkaline reaction, which is caused by loss of carbon dioxide.

Certain soaps have an adjuvant action on the acriflavine titer. Of the soaps tested, oleates were found most adjuvant for the streptococcus, lurates for the staphylococcus and palmitates for the typhoid bacillus.

The metabolic products of the streptococcus here studied antagonize the germicidal action of acriflavine.

The germicidal action of acriflavine is diminished greatly by pus. This is partially the effect of the acidity of the pus, partially the effect of the cells, fibrin and autolytic products that are present.

A method of treating experimental streptococcus empyema in rabbits was evolved. While this gave some encouraging results, it failed to save any infected animals. This lack of success seemed due to the high virulence of the test organism. The results indicate that acridine dyes, especially when combined with an appropriate soap, would be useful in treating infections that do not tend to become generalized rapidly.

AUTHOR'S SUMMARY.

UNSUCCESSFUL EXPERIMENTS WITH MERCUROCHROME AS A BILIARY ANTISEPTIC: IX. EXPERIMENTAL TYPHOID-PARATYPHOID CARRIERS. K. F. MEYER, H. SOMMER and B. EDDIE, J. Infect. Dis. **38**:469, 1926.

Mercurochrome-220 soluble intravenously injected is excreted in the hepatic bile of rabbits in concentrations which may destroy 10,000,000 typhoid bacilli in from six to twenty-four hours. However, it has been impossible to cure experimentally produced gall-bladder carriers by giving mercurochrome intravenously or by mouth.

The colorimetric methods used in the estimation of mercurochrome, the influence of proteins, etc., on the germicidal properties of the compound are discussed.

AUTHORS' SUMMARY.

A BACTERIOLOGIC STUDY OF CHRONIC PERIAPICAL DENTAL INFECTION. RUSSELL L. HADEN, J. Infect. Dis. **38**:486, 1926.

The results of periapical cultures from 1,500 incisor, cuspid and bicuspid teeth are reported.

All cultures have been made in deep tubes of glucose brain broth and glucose brain agar, which affords most favorable nutritive conditions, varying oxygen tension and allows the number of bacteria to be estimated.

Vital teeth have been cultured in a routine manner to determine the chances of error in technic.

The quantitative results of cultures from different types of teeth are given.

For comparative purposes the number of tubes containing ten or more colonies is most valuable. Four and eight tenths per cent of the vital group, 62.8 per cent of the pulpless teeth with positive roentgenograms and 46.2 per cent of the pulpless teeth with negative roentgenograms showed ten or more colonies per tube.

The nonhemolytic streptococcus is by far the most commonly found organism. Hemolytic streptococci occur only rarely.

The most common types of streptococci as determined by carbohydrate fermentation are the fecalis, mitis and salivarius.

AUTHOR'S SUMMARY.

FERMENTATION OF CELLOBIOSE BY THE COLI-AEROGENES GROUP. STEWART A. KOSER, J. Infect. Dis. **38**:506, 1926.

On reviewing the entire collection of cultures it is evident that so far as the two well defined sections of the group are concerned, there appears to be an almost perfect correlation of tests; the intestinal *Bacterium coli* is quite distinct from the well-known aerogenes-cloacae forms. When certain other members of the group obtained from soil are considered, especially the "intermediate" type and the irregular forms, the same striking correlation between all of the tests is not apparent. There is, however, a marked correlation between source and the results of the citrate and cellobiose tests. These tests appear to be more significant than the methyl red and Voges-Proskauer tests in indicating the source of the cultures. Again the point is emphasized, as in previous work, that there is no justification in assigning a fecal origin to all methyl red positive cultures which may be encountered in soil or other sources outside the animal body.

AUTHOR'S SUMMARY.

A METHOD OF INCREASING THE VIRULENCE OF CULTURES OF CLOSTRIDIUM CHAUVOEI BY THE USE OF FERRIC SALTS. JOSEPH P. SCOTT, J. Infect. Dis. **38**:511, 1926.

Experiments with many strains of *Clostridium chauvoei* have shown the difficulty of maintaining the virulence of these organisms.

The addition of ferric sulphate to culture media stimulated these organisms to such an extent that avirulent strains regained their virulence.

The virulence of *Cl. chauvoei* is independent of the fermentative or antigenic properties.

These results are thought to confirm the presence of the so-called "lethal substance" or specific cellular activity of virulent cultures of *Cl. chauvoei*.

AUTHOR'S SUMMARY.

THE INCIDENCE OF PNEUMOCOCCUS TYPES IN THE PNEUMONIAS OF CHILDREN.
RUTH E. WESTLUND, J. Infect. Dis. **38**:514, 1926.

In a series of sixty-nine cases of lobar pneumonia and thirty-four cases of bronchopneumonia occurring in children between the ages of 3 weeks and 11 years, pneumococci were obtained by nasopharyngeal swabbing in 60.8 per cent of the cases of lobar pneumonia and in 52.6 per cent of the cases of bronchopneumonia.

The relative incidence of pneumococcus types in these two groups of cases was much the same, group 4 predominating, type 2 coming next in frequency, type 1 third, and type 3 being least frequent. The fixed types of pneumococcus are less frequent in the pneumonias of children than in those of adults. The association of group 4 with representatives of one or another of the fixed types was demonstrated in several instances.

In a group of thirteen cases of nonpneumonic respiratory disease in children, pneumococci were present in 92.0 per cent. No examples of types 1 and 3 were encountered, type 2 and group 4 forming one third and two thirds, respectively, of isolated pneumococci.

In forty-eight nonrespiratory diseases in children, pneumococci were found in 58.0 per cent. Type 1 was not represented in this group, type 2 formed 14.2 per cent, type 3, 3.6 per cent and group 4, 82.1 per cent. The occurrence of type 2 pneumococci in the throats of these children in the hospital wards may have been due to contact.

AUTHOR'S SUMMARY.

REMOVAL OF ACIDFASTNESS FROM TUBERCLE BACILLI BY OLEIC ACID OR OLIVE OIL.
F. A. McJUNKIN, J. Infect. Dis. **38**:520, 1926.

Cultures of tubercle bacilli dehydrated with acetone or alcohol lose their acidfastness on incubation with oleic acid. Cultures dehydrated with acetone lose their acidfastness on incubation with olive oil, but those dehydrated with alcohol do not. The loss of acidfastness is incomplete in either case with less than 1 per cent of the bacilli retaining their property of staining red by the Ziehl-Neelsen method. The few bacilli that remain acidfast are thought to be dead at the time of incubation.

Traces of water are necessary for the discharge of acidfastness. The water adheres to the dehydrated cultures in the oily medium.

The temperature at which the loss of acidfastness takes place most rapidly is 37 C. with an abrupt cessation at a lower temperature at which the metabolic activities of the bacilli are greatly reduced and at temperatures above 37 C. which approach the thermal deathpoint of the cultures. The variations in the reaction with changes in temperature are not those to be expected were the process a simple chemical one.

AUTHOR'S SUMMARY.

TUBERCULOUS INFECTION IN GUINEA-PIGS TREATED WITH TUBERCLE BACILLI MADE NONACIDFAST BY INCUBATION WITH OLIVE OIL. F. A. McJUNKIN, J. Infect. Dis. **38**:524, 1926.

Tuberculous infection of guinea-pigs produced by inoculation with virulent tubercle bacilli (Saranac Laboratory H60) is not influenced by injections of saline suspensions of cultures of the same strain of bacilli made nonacidfast by dehydration and incubation with olive oil. The results are the same whether the injection of nonacidfast suspensions precedes or follows the inoculation.

Mixtures of nonacidfast tubercle bacilli of a lesser virulence (Saranac Laboratory H37) and the olive oil in which they were incubated were injected

into several series of guinea-pigs before inoculation with living cultures of the same strain of organism. The animals treated with the oil-bacillus suspensions became tuberculous on incubation and there was no material difference in the progress of the infection in the treated guinea-pigs and untreated ones of the same age and weight.

AUTHOR'S SUMMARY.

TULEREMIA IN WILD RATS. L. V. DIETER and BERNICE RHODES, J. Infect. Dis. **38**:541, 1926.

The existence of latent *Bacterium tularense* infections in wild rats has been established by inoculation experiments, by cultures on egg yolk medium and by agglutination tests. The lesions in the naturally infected rats are not characteristic and the nature of the infection can be established only by inoculations of guinea-pigs.

AUTHORS' SUMMARY.

EXPERIMENTS ON THE INFLUENCE OF FATIGUE ON INFECTION. A. E. BOYCOTT and C. PRICE-JONES, J. Path. & Bact. **29**:87, 1926.

The authors attempted to determine experimentally the influence of fatigue on infection in the black and white and the albino rats. Rats were fatigued in revolving drums until exhausted; one group of thirty-four animals were then inoculated with a culture of Gaertner's bacillus of known virulence. Twenty-three animals died as a result of the treatment, while twenty-two of the control animals that had not been fatigued also died.

In another set of experiments, forty-one rats were inoculated with Gaertner's bacillus and then exhausted by exercise on each of several days following. Twenty-nine of these rats died as compared with twenty-four of the controls.

Animals that were fatigued and then fed cultures of Gaertner's bacillus gave different results. The fatigued animals became very ill, exhibiting diarrhea and cyanosis, and half of them died. Of the control animals which received similar feedings of bacteria but were not fatigued, only one became ill, and none died. Gaertner's bacillus was found in the spleens of both fatigued and normal rats, but in some way fatigue increased the illness and mortality.

The authors also investigated the effect of fatigue in relation to infection with tubercle bacilli. Thirty-six rats were used in the experiment—twelve were inoculated with human and twelve were inoculated with bovine tubercle bacilli. Half of each lot and half of the controls were fatigued fifteen times over a period of eight weeks, when they were killed and examined. This amount of exercise failed to break down the natural resistance of the rat to tuberculosis.

E. M. HALL.

THE OCCURRENCE OF BRUCELLA ABORTUS AND MYCOBACTERIUM TUBERCULOSIS IN COW'S MILK. G. S. WILSON and MURIEL M. NUTT, J. Path. and Bact. **29**:141, 1926.

Guinea-pig inoculation of 488 samples of cow's milk were made. Acid-fast bacilli were found microscopically in sixty-eight pigs but no saprophytic acid-fast bacilli could be cultivated from any of them. This is important since Rabinowitsch found that of ninety specimens of butter 23 per cent produced a disease in guinea-pigs macroscopically indistinguishable from tuberculosis. Acid-fast bacilli were found microscopically in the lesions, but on cultivation

they proved to be butter bacilli. Wilson and Nutt concluded from their results that if in the lesions in a guinea-pig into which milk had been injected acid-fast bacilli are found, the milk contains tubercle bacilli.

In guinea-pigs into which milk had been injected and which had been killed three weeks after inoculation, nontuberculous lesions of the lymphatic glands, usually of the sublumbar, were found. *Brucella abortus* was cultivated from about one third of these glands. Not infrequently in guinea-pigs receiving these injections growing *Brucella abortus* was found in association with the tubercle bacillus, probably a chance relationship. The calculation is made that 5.7 per cent of the samples of single milk and 8.8 per cent of the samples of mixed milk contained *Brucella abortus*, while 13 per cent of the samples of mixed milk contained the tubercle bacillus.

E. M. HALL.

SIX CASES OF LABORATORY INFECTION OF TULAREMIA IN MAN. R. R. PARKER and R. R. SPENCER, Pub. Health Rep. 41:1341, 1926.

This report increases to seventeen the total number of cases in laboratory workers, fourteen of which have occurred in the laboratories of the U. S. Public Health Service, and three in the Lister Institute of Preventive Medicine in London. In all the seventeen cases the infection entered the body without any evidence of a local lesion and without causing glandular enlargement. In each case the clinical picture resembled that of typhoid fever.

THE SUSCEPTIBILITY OF THE COYOTE TO TULAREMIA. R. R. PARKER and EDWARD FRANCIS, Pub. Health Rep. 41:1407, 1926.

Three young coyotes, from 4 to 6 months of age, were infected with acute tularemia by feeding them the tissues of Belgian rabbits and guinea-pigs just dead from typical infections. Death occurred, respectively, fifty-three, twenty-two and thirteen days after the first feeding of infectious material. The course of infection in each case was attended by loss of appetite, and by an increasing weakness and emaciation. At necropsy the tissues showed no gross pathologic lesions such as are characteristic of acute tularemia in laboratory animals. Diagnosis was made by the following observations: (a) the coyote serums did not show specific agglutinating properties for *Bacterium tularense* before the first feeding of infectious material, but did give specific reactions beginning the second week thereafter; (b) typical acute tularemia infection was produced in guinea-pigs injected with emulsions of necropsy material from each coyote, and (c) pure cultures of *Bacterium tularense* were isolated from the tissues of guinea-pigs in which the infection from the coyotes was propagated.

The recovery of typical tularemia from the salivary glands of two of the experimental coyotes indicates the possibility of human infection by the bite of an infected coyote. Besides the case noted as evidently caused by this, another case reported by Dr. C. T. Pigot of Roundup, Mont., also in 1925, was apparently due to infection by the bite of a ground squirrel.

These data are of especial interest as indicating a hitherto unsuspected avenue for the transfer of tularemia infection from its normal hosts to man; namely, by the bite of a wild rodent or carnivore.

The susceptibility of coyotes and the evident possibility of fatal infection suggest that tularemia may be a factor, at least, in the diminution of the abundance of coyotes which is so frequently noted following the decimation of rabbit populations in the same localities.

AUTHORS' SUMMARY.

ROCKY MOUNTAIN SPOTTED FEVER: CERTAIN CHARACTERISTICS OF BLOOD VIRUS.
R. R. SPENCER and R. R. PARKER, Pub. Health Rep. 41:1817, 1926.

The serum from guinea-pigs infected with Rocky Mountain spotted fever and subjected to high speed (8,800 revolutions per minute) centrifugalization retains infectivity in the top portion.

After repeated washings by slow speed (1,200 revolutions per minute) centrifugalization, red and white blood cells from infected guinea-pigs are capable of transmitting the infection, although the demonstration of organisms in fresh preparations or stained smears of such cells is extremely rare.

Normal red and white blood cells to which serum virus has been added retain the infection after repeated washings by centrifugalization.

A suspension of platelets from an infected guinea-pig, as well as a suspension from a normal animal to which virus has been added, does not retain the infection after washing by centrifugalization.

Suspensions of fullers' earth or charcoal to which serum virus has been added, quickly lose infectiousness when washed by centrifugalization.

The suggestion is made that the virus of Rocky Mountain spotted fever may assume a form incapable of demonstration by known methods.

AUTHORS' SUMMARY.

THE EFFECT OF SANOCRY SIN ON BACILLUS TUBERCULOSIS. R. M. FRY, Brit. J. Exper. Path. 7:176, 1926.

In normal human or ox blood or plasma mixed with sodium aurothiosulphate in vitro, concentrations of sodium aurothiosulphate up to 1 in 2,500 had no effect on the growth of the tubercle bacillus. Above this concentration the results are rather variable, but in some cases good growth was obtained in concentrations up to 1 in 250, and in one case as high as 1 in 50. The bacillus grows as readily in the plasma of a tuberculous patient taken ten minutes or two days after a dose of 1 Gm. of sodium aurothiosulphate as in the plasma drawn before the dose, or in normal human plasma. The bacillus grows as readily in the plasma of a rabbit after a dose of sodium aurothiosulphate equivalent to 3 Gm. in a human being as in the plasma drawn before the injection.

S. A. LEVINSON.

MECHANISM OF DAUGHTER CYST FORMATION IN HYDATID DISEASE. H. R. DEW, M. J. Australia 1:451, 1926.

The daughter cysts in a typical hydatid cyst have an endogenous origin only, arising by progressive evolution of the cells of the original germinal membrane or from brood capsules. More rarely they may develop from scolices. From thin walled daughter cysts, granddaughter cysts may arise in another way, namely, by an external herniation of both layers at weakened parts of the laminated coat with secondary exclusion of the pouch. Exogenous daughter cyst production from intracuticular nuclear masses, as usually described, does not occur. In secondary omental cysts, in bone and in the viscera of herbivora, peculiar cysts form which are due to external herniation of both layers with secondary closure and cyst formation, such herniations being dependent on the nature of the adventitious tissues. Secondary echinococcosis is a well established fact and may occur in the abdomen, in the pleura or in operation wounds as the result of implantation of daughter cysts, brood capsules or scolices. Hydatid emboli and metastases can occur after intravascular rupture of cysts with carriage of brood capsules or scolices by the blood stream and their survival and growth in new situations. This is the explanation of most cases of multiple cysts of the lungs, heart and brain.

EXPERIMENTAL TRANSMISSION OF ORIENTAL SORE TO MAN BY PHLEBOTOMUS PAPATASSII (SCOPOLI). E. SERGENT, L. PARROT, A. DONATIEN and M. BEGNET, Ann. de l'Inst. Pasteur. **40**:411, 1926.

Phlebotomus papatassi (a blood sucking sand flea) was found to harbor *Leishmania tropica*. Macerated bodies of these insects infected one person with the formation of a lesion typical of oriental sore. White mice and dogs were infected with the strain isolated in this case.

G. B. RHODES.

A NOTE ON THE CHARACTERISTICS OF A MICRO-ORGANISM BELONGING TO A SALMONELLA GROUP, ISOLATED FROM AN EPIZOOTIC AMONG RATS AND GUINEA-PIGS. I. GHEORGIN, Ann. de l'Inst. Pasteur. **40**:447, 1926.

A serologic study of this organism places it in the enteritidis group of *Salmonellae*.

G. B. RHODES.

SPRUE IN GEORGIA. C. MIKELADZÉ, Bull. Soc. de path. exot. **19**:201, 1926.

Sprue has never been described in the Near-Orient. Mikeladzé investigated ten cases of sprue which he has observed in the medical clinic of the University of Tiflis (Georgia, Caucasus) from September, 1923, until spring, 1925.

The patients' complaints in these cases were usually persistent diarrhea, progressive loss of weight and sore tongue. On examination the patients were ordinarily very pale with a characteristic earthy nuance of the skin. The temperature was subnormal; the gastric juice lacked free hydrochloric acid; the tongue was red and smooth with a gray metallic steel-like glint. The reaction of the sputum was acid and it did not give the potassium sulphocyanide reaction. There was a marked anemia with a low red cell count, and with a hemoglobin index below one. There was also a leukopenia concerning only the polymorphonuclear neutrophils. The disease in Mikeladzé's cases showed definite remissions at which time almost all symptoms disappeared. Two of these cases which came to necropsy showed a follicular enteritis with atrophy of the mucosa of the digestive organs. Aphthous ulcerations covered the surface of the tongue and the esophagus, and there was atrophy of the liver. In the ten cases studied one patient was a carrier of cysts of *Entamoeba dysenteriae*, one of *Trichomonas intestinalis*. Two had chronic malaria.

B. M. FRIED.

CULTURE OF THE SPIROCHETE FROM TUBERCULOUS HEMOPTYSIS. F. BEZANSON and E. ETCHGOIN, Compt. rend. Soc. de biol. **94**:1056, 1926.

In 1923 Etchegoin described a spirochete found by him in the sputum of tuberculous patients with hemoptysis. This report concerns itself with an artificial medium on which the spirochete grows. Its composition is as follows: horse serum, 200 cc.; physiologic sodium chloride solution, 8.5 per 1,000, 800 cc.; peptone water, 3 per cent, 200 cc.

This is filtered on a Chamberland L³ filter, and distributed in test tubes, 12 cc. in each, containing 1.5 cc. of sterile petrolatum. The medium is sterilized at 56 C. for thirty minutes on three successive days. After ten days at 37 C., there is a luxurious culture of the micro-organism, which also has been transplanted successfully five times.

The spirochete examined under the ultramicroscope shows the usual spirochetal movements and, analogous to other spirochetes, divides transversally.

It measures from 7 to 13 microns in length and from 1 to 2 microns in width. It contains from 4 to 5 spirals which are rather close to each other.

B. M. FRIED.

SOME EXPERIMENTS IN REGARD TO THE ACTION OF SANOCRY SIN ON TUBERCLE BACILLI AND THE EXPERIMENTAL TUBERCULOSIS IN GUINEA-PIGS AND RABBITS. A. CALMETTE, A. BOQUET and L. NÈGRE, *Rev. de la tuberc.* 7:169, 1926.

There was complete bacteriostatic action in glycerole broth up to 1:1,000, at 1:1,000,000 no effect. A 2 per cent solution has no bactericidal action during seven and one-half hours of contact; marked but not complete effect after thirty hours of contact. The effect of intravenous treatment with sanocrysin had no effect on the development of experimental tuberculosis in rabbits and guinea-pigs. No specific toxic substance is liberated by the action of the salt on tubercle bacilli in vitro. Sanocrysin given by mouth is only slightly more toxic for tuberculous than for normal animals. The "anti-tuberculous" serum, advised for the prevention of "sanocrysin shock" does not modify the toxicity of tuberculin for tuberculous animals.

MAX PINNER.

COMPARISON BETWEEN THE ACTION OF SANOCRY SIN AND TUBERCULIN ON NORMAL AND TUBERCULOUS GUINEA-PIGS. E. FERNBACH and G. RULLIER, *Rev. de la tuberc.* 7:300, 1926.

The toxicity of sanocrysin is only slightly higher for tuberculous than for normal guinea-pigs, the toxic action being essentially the same: congestion of lymph glands and internal organs and renal hemorrhages; in localization and intensity these changes seem to be independent of tuberculous foci, whereas similar changes due to tuberculin in tuberculous animals are quantitatively strictly dependent on the extent of tuberculous tissue. The local reaction at the site of injection is totally different from the local tuberculin reaction, but is apparently identical with the local lesion produced by sodium hyposulphite. "Anti-tuberculous" serum which is capable of preventing death by sanocrysin shock has no effects on tuberculin shock. The conclusion is that there is no similarity between the action of sanocrysin and tuberculin on the tuberculous organism.

MAX PINNER.

ON THE "LIFE CYCLE" OF BACTERIA: A CONTRIBUTION TO THE STUDY OF THE GRANULAR FORM. A. FONTES, *Mem. do Inst. Oswaldo Cruz* 18:197, 1926.

The bacteria studied are nucleate cells. The nucleus of these cells is dispersed, affecting chromidium form which with the evolution of the bacterium toward reproductive activity mobilizes and condenses into granulations. The localization at the poles indicates an amitotic process, the details of which cannot be followed up because of the unsatisfactory nature of the apparatus used for observation. The irregular distribution of the chromidial substance inside bacterial cells, in the same manner as its regular distribution in cells of the same nature, seems to indicate that cells of the same species are able to divide and multiply by different processes. The growth of these cells and their reproduction are closely connected with the growth and reproduction of the chromidial corpuscles. The growth and reproduction of these cells takes place through the emission of granules inside the protoplasm, disposing themselves for the ulterior division of the cell, or else through the emission

of granules outside the organism studied, which will give rise to a new reticulum about to build up a newly formed cell. The growth and reproduction of these cells may take place in the length direction or laterally, providing for transverse planes of division (cocci, coli and dysentery bacilli) or longitudinal planes of division like the branching of a tree (diphtheria and tubercle bacilli sometimes *B. coli*).

AUTHOR'S SUMMARY.

INVISIBLE AND UNCULTURABLE FORMS OF PATHOGENIC BACTERIA (KRYPTANTIGENIC VIRA). E. FRIEDBERGER, Klin. Wchnschr. 5:782, 1926.

The specific cause of typhus may exist in two forms: as the bacillus, and as a neither visible nor culturable form, recognizable, at present, only through its pathogenic and antigenic activity. The invisible form may be the more pathogenic.

ARTHUR LOCKE.

THE DICK REACTION AND SCARLET FEVER VACCINATION WITH STREPTOCOCCUS VACCINE. B. VAS, Klin. Wchnschr. 5:1232, 1926.

The specificity of the Dick test for susceptibility to scarlet fever is confirmed. No conclusion is drawn as to the value of the vaccination.

ARTHUR LOCKE.

INTESTINAL ANTHRAX. W. VILLINGER, Virchows Arch. f. path. Anat. 260:484, 1926.

This is the report of a case of fatal primary intestinal anthrax infection, in which the preoperative diagnosis was acute pancreatitis. The clinical manifestations were those of acute peritonitis without localizing symptoms, leukocytosis, marked toxemia, weak pulse and subnormal temperature. The postmortem examination revealed an ulcer just above the ileocecal valve and another small one in the duodenum.

O. T. SCHULTZ.

THE PRIMARY INVOLVEMENT IN TUBERCULOSIS. P. SCHÜRMANN, Virchows Arch. f. path. Anat. 260:664, 1926.

Schürmann devotes a 193 page monograph to a discussion of the natural history of the tuberculous process, and to a minute analysis of the published and personal data relating to the conception of Ranke that the primary focus of infection always manifests itself by regional lymph node involvement, the chief evidence of which in later or healed stages of the disease is calcification. Schürmann's own material consisted of 1,000 unselected necropsies—those of children under 3 weeks of age being excluded—which were minutely and thoroughly examined for the evidence of healed tuberculosis, especial attention being paid to lymph nodes, with a thorough search for the primary focus if calcified lymph nodes were found. How painstaking, one might almost say meticulous, this search was is evident from the author's statement that he frequently had bodies removed from the casket for further examination after careful search of the lungs and the attached bronchial and mediastinal lymph nodes had failed to reveal any evidence of tuberculosis. The relation of secondary foci, whether healed or active, to the primary complex was also investigated. Before beginning his series of 1,000 cases he discarded 150 examinations, because he had found that his success in detecting evidences of tuberculosis depended on his own experience, since in the first fifty necropsies

he had positive results in only 56 per cent, and in the next 100 in 77 per cent, whereas in the next 100 his figures approached those of Burkhardt, Naegeli, Reinhardt, Puhl and others, who had found evidence of tuberculosis in from 91 to 98 per cent of all necropsies. In eighty-eight necropsies of persons under 18 years of age, Schürmann found anatomically detectable tuberculosis in 58 per cent, and in 912 persons over 18 years old in 92 per cent. Fibrosis of the lungs or pleura without calcification or microscopic tuberculosis of regional lymph nodes was not accepted as evidence of tuberculosis. If such changes were present in the regional lymph nodes, then fibrosis or scars of the lung or pleura were accepted as part of the primary complex. Of his anatomically positive 855 cases, the primary complex was pulmonary in 85 per cent and multiple in 8 per cent. The multiple primary infections helped to give 20 per cent of cases with an extrapulmonary primary complex. In the cases with a pulmonary primary complex the localization was in the right lung in 54 per cent, the figures for the individual lobes being, upper 28 per cent, middle 6 per cent, and lower 20 per cent; in the left lung in 46 per cent, with 26 per cent in the upper lobe, and 20 per cent in the lower. Of his anatomically positive cases the primary complex could not be found in 4 per cent, which is interpreted as indicating, not that it was not present, but inability to find it. In 38 per cent of the positive cases the primary complex was the only evidence of infection detected. In 62 per cent there were other foci, either quiescent or active, which had arisen from the primary focus. Schürmann concludes that the literature of experimental and human tuberculosis and his own investigation prove the correctness of Ranke's assertion that in almost 100 per cent of persons it is possible to find the anatomic primary complex of tuberculosis and that in almost every case of tuberculosis it is possible to detect the primary focus. The bibliography includes 312 references.

O. T. SCHULTZ.

EXPERIMENTAL TYPHUS: IV. FILTRABILITY OF VIRUS OF TYPHUS. I. W. HACH, Ztschr. f. Hyg. u. Infektionskrankh. **106**:221, 1926.

Hach filtered a suspension of organs of seven guinea-pigs infected with the virus of typhus through a Chamberland "F" filter. He injected the filtrate into fourteen guinea-pigs and produced a typical attack of fever in all of them. Histologic examination revealed the presence of cellular nodules in various organs. Hach believes that the animals receiving injections contracted a light attack of typhus fever.

W. OPHÜLS.

EXPERIMENTAL SCARLET FEVER. I. W. HACH and N. P. BORDZILOWSKAJA, Ztschr. f. Hyg. u. Infektionskrankh. **106**:232, 1926.

The authors injected from 3 to 5 cm. of blood taken from three patients with scarlet fever on the second or third day of the disease intraperitoneally into eleven guinea-pigs. Five animals developed an attack of fever and an enlargement of the spleen. No streptococci were present in the blood used for the injection or in the tissues of the diseased animals. They do not contend that the disease produced in the experimental animals is equivalent to scarlet fever but they believe that the results are sufficiently suggestive to warrant further experimentation along these lines.

W. OPHÜLS.

Immunology

ACQUISITION AND LOSS OF HYPERSENSITIVENESS IN EARLY LIFE. HAROLD G. STUART and MARYNIA FARNHAM, *Am. J. Dis. Child.* **32**:341, 1926.

Evidence is presented to confirm the general impression that hypersensitivity to food proteins is most commonly encountered in early childhood, and that there is a natural loss of sensitivity to these substances during childhood. The age at which such loss will take place, is, however, not predictable. No case could be found showing definitely the development of a specific food idiosyncrasy.

Figures are given showing the rarity of hypersensitivity to inhalant proteins in infants, and that the number of cases encountered increases rapidly during the middle period of the first decade. Cases are cited which strongly suggest the acquisition of specific inhalant sensitizations.

The inference is drawn that hypersensitivity to food proteins tends to be present at birth and to be lost gradually during childhood, whereas hypersensitivity to inhalant proteins tends to be acquired and is more resistant to change.

A changing state of sensitization is to be expected, therefore, during childhood, and protein tests should be repeated frequently to obtain the best results with treatment.

Excessive exposure to inhalant proteins which show negative skin tests should be avoided in the asthmatic child.

Active treatment by oral desensitization of subjects found to react to important food substances is preferable to awaiting the natural loss of such hypersensitivity.

AUTHORS' SUMMARY.

PASSIVE ANAPHYLAXIS IN A HEMOPHILIAC. C. A. MILLS and L. SCHIFF, *Am. J. M. Sc.* **171**:854, 1926.

The induction of a skin reaction toward foreign protein causes the clotting time of hemophiliac blood to fall promptly to normal. If bleeding is in progress, it stops completely. The effect persists for long periods and may be repeated as frequently as needed. The bleeding of a hemophiliac patient who proved refractory to sensitization toward horse serum was checked by transfusion of blood from a known sensitive person.

ARTHUR LOCKE.

ADENOMAS OF THE ISLANDS OF LANGERHANS. SHIELDS WARREN, *Am. J. Path.* **2**:335, 1926.

Four cases of adenomas of the islands of Langerhans are presented, bringing the number of reported cases up to twenty. These tumors are characterized by resemblance to the islands in arrangement of their cells and in appearance of the individual cell, by absence of mitotic figures, by the presence of a definite capsule and by compression of the adjacent tissue. They are not so rare as the small number of reported cases would lead one to believe.

AUTHOR'S SUMMARY.

MALIGNANT NEOPLASMS OF THYROID. W. M. SIMPSON, *Ann. Clin. Med.* **4**:643, 1926.

Fifty-five cases were studied, fifty of which were carcinomas and five sarcomas. More than 60 per cent of the carcinomas were unsuspected before

microscopic examination; in about one half of the cases there were signs of hypothyroidism. A relatively rapid increase in size and hardness in a quiescent or slowly growing goiter in a person over 30 years of age is suspicious.

PRIMARY THYROID CARCINOMA SIMULATING HYPERNEPHROMA. W. M. SIMPSON, *Ann. Clin. Med.* **4**:668, 1926.

There is a form of thyroid carcinoma that simulates the structural characteristics of hypernephromas.

GASTRIC ULCER: IV. EXPERIMENTAL PRODUCTION OF GASTRIC ULCER BY LOCAL ANAPHYLAXIS. P. F. SHAPIRO and A. C. IVY, *Arch. Int. Med.* **38**:237, 1926.

The authors produced gastric ulcer experimentally on the basis of local anaphylaxis to specific antigens. Passively immunized animals yielded the same gastric lesions. Acute ulcers in rabbits usually healed in about twelve days. Precipitins to plant or to animal proteins could not be detected in sensitized dog's serums. In dogs the gastric reaction was more severe than the cutaneous and in rabbits the reverse was true. Positive results were obtained in rabbits and dogs with egg albumin, beef protein, oat protein, squash seed globulin, edestin, hemoglobin and horse serum; negative results with casein, milk and tuberculin.

S. A. LEVINSON.

IMMUNOLOGICAL STUDIES WITH HERPES VIRUS WITH THE CONSIDERATION OF THE HERPES-ENCEPHALITIS PROBLEM. HANS ZINSSER and FEI-FANG TANG, *J. Exper. Med.* **44**:21, 1926.

Observations support the view that the herpetic virus is intracellular—located in the infected nervous system. Neutralization of the virus with serum of actively immunized animals is possible; it is probable that the irregular results usually reported may be due, not to variations in the potency of the serum, but to the inaccessibility of the intracellular virus. Passive immunization uniformly failed, and active immunization was attained only when a certain degree of reaction to living virus occurred. Herpes virus was never successfully transferred directly from man to rabbits, and animals treated with human encephalitis material failed to develop immunity as evidenced by later herpes inoculations, but the characteristic herpetic syndrome in rabbits was modified to simulate many of the clinical features of encephalitis in man. All the evidence obtained by direct inoculations made the identity of the two viruses herpes and epidemic encephalitis seem unlikely.

AUTHORS' SUMMARY.

THE SKIN RESPONSE OF RABBITS TO NONHEMOLYTIC STREPTOCOCCI. I. DESCRIPTION OF A SECONDARY REACTION OCCURRING LOCALLY AFTER INTRADERMAL INOCULATION. C. H. ANDREWES, C. L. DERICK and HOMER SWIFT, *J. Exper. Med.* **44**:35, 1926.

Certain streptococci and a few pneumococci, when injected intradermally into rabbits, produce not only a reaction within the first twenty-four to forty-eight hours, but also, in about 50 per cent, a secondary reaction on the eighth or ninth day. Hemolytic streptococci, staphylococci, *Micrococcus catarrhalis* or *Bacillus coli* do not cause this secondary reaction, nor do the last three cause inhibition of the reaction, as do both hemolytic and nonhemolytic streptococci

and pneumococci if injected before the test injection with green streptococci. Killed streptococci are less effectual. Guinea-pigs did not produce a secondary reaction. The causative agent has not been determined. It may be a form of allergic reaction.

ETHEL B. PERRY.

THE SKIN RESPONSE OF RABBITS TO NONHEMOLYTIC STREPTOCOCCI: II. ATTEMPTS TO DETERMINE WHETHER THE SECONDARY REACTION IS OF THE NATURE OF AN ARTHUS PHENOMENON. C. L. DERICK and C. H. ANDREWES, *J. Exper. Med.* **44**:55, 1926.

Attempts to influence the appearance of the secondary reaction in rabbits after intradermal injections of green streptococci by injections of immune serums either locally or intravenously at different times with relation to the expected reaction, and also attempts to correlate the secondary reaction with demonstrable antibody (agglutinin) formation failed to support an interpretation of the reaction as analogous to the Arthus phenomenon. It seemed probable that this reaction may be more closely allied to the tuberculin reaction.

ETHEL B. PERRY.

THE RÔLE OF THE RETICULO-ENDOTHELIAL SYSTEM IN IMMUNITY: III. THE PRODUCTION OF ACTIVE AND PASSIVE ANAPHYLAXIS IN THE BLOCKED ANIMAL. C. W. JUNGBLUT and J. A. BERLOT, *J. Exper. Med.* **44**:129, 1926.

Guinea-pigs receiving intravenous injections with massive doses of India ink before active sensitization occasionally exhibited a more or less marked decreased sensitiveness to the reinjection of the antigen.

The serum of rabbits which had received massive doses of India ink before the sensitizing injections, showed approximately the same titer of anaphylactic antibodies as that of sensitized normal control animals, as demonstrated by the degree of passive sensitization induced in guinea-pigs.

The precipitin titer of sensitized rabbits blocked with massive doses of India ink was somewhat lower than that of sensitized normal controls. In one instance, the intravenous injection of smaller doses of India ink was followed by a higher precipitin titer. No uniform relation was found between the height of the precipitin titer and the anaphylactic power of the antisera.

One blocking injection of India ink given to guinea-pigs before passive sensitization did not interfere with the occurrence of anaphylactic shock nor alter its nature.

AUTHORS' SUMMARY.

STUDIES ON THE OXIDATION AND REDUCTION OF IMMUNOLOGICAL SUBSTANCES. J. M. NEILL, *J. Exper. Med.* **44**:199, 1926.

Pneumococcus hemotoxin, an antigenic substance of bacterial origin, is converted by oxidation to a product devoid of hemolytic action. The oxidation product of the hemotoxin may be converted to the original hemolytic substance by reduction, by the anaerobic action of certain bacteria or by sodium hydro-sulphite. The active lysin, or hemotoxin, produced by the reduction of the inactive oxidized extracts is identical with the original, active, reduced hemotoxin; it possesses the same degree of thermolability and is neutralized by the same specific antibody. The inactive products formed by heating the hemotoxin anaerobically cannot be "reactivated" by reducing agents. The immunologic significance of these relations will be discussed in a subsequent paper.

AUTHOR'S SUMMARY.

STUDIES ON THE OXIDATION AND REDUCTION OF IMMUNOLOGICAL SUBSTANCES:
II. J. M. NEILL, J. Exper. Med. **44**:215, 1926.

A study has been made of the oxidation and reduction of the hemotoxin of the Welch bacillus. The oxidation of the lysin results in the loss of its hemolytic activity. The "inactive" oxidation product of the Welch lysin may be reversed to the "active" lysin by treatment with biologic or chemical reducing agents. The lysin, both in its reduced and in its oxidized form, is irreversibly inactivated by the same heat treatment. The p_n of the system is an important factor in the oxidation of the lysin, the process proceeding much more rapidly at a p_n above 7.0.

AUTHOR'S SUMMARY.

STUDIES ON THE OXIDATION AND REDUCTION OF IMMUNOLOGICAL SUBSTANCE: III.
J. M. NEILL, J. Exper. Med. **44**:227, 1926.

A preliminary study was made of the rate of formation of tetanolysin and of the effect of glucose on the lysin production. Tetanolysin appearing early in cultural growth is, like the Welch lysin, to be distinguished from the endocellular hemotoxin of pneumococci. Organisms named in order of the increasing heat resistance of their hemotoxins are the pneumococcus, cholera vibrio, Welch bacillus and then tetanus: the tetanolysin is inactivated in ten minutes at 65 C. Tetanolysin inactivated by aeration may be partly reactivated by reduction but irreversible degradation products are also formed which may be estimated by the same methods that have been used in the study of hemoglobin and its derivatives in deteriorating solutions of blood pigments.

AUTHOR'S SUMMARY.

STUDIES ON THE OXIDATION AND REDUCTION OF IMMUNOLOGICAL SUBSTANCES: IV.
J. M. NEILL and T. B. MALLORY, J. Exper. Med. **44**:241, 1926.

The "spontaneous deterioration" of streptolysin has been studied by the methods already used in investigations of the oxidation-reduction of blood pigments and of the lysins of other bacteria. From the results of this study, it may be concluded that the commonly observed "spontaneous deterioration" of streptolysin consists in the conversion of the originally active lysin to a hemolytically inactive oxidation product. This process is a reversible one, and the activity of the lysin is restored by reduction.

AUTHORS' SUMMARY.

THE SEROLOGICAL CLASSIFICATION OF HEMOLYTIC STREPTOCOCCI OBTAINED FROM
CASES OF SCARLET FEVER. J. SMITH, J. Hyg. **25**:165, 1926.

Hemolytic streptococci have been obtained from throat cultures in 92 per cent of cases of scarlet fever in the first two days of the disease. Strains from 210 cases were found to belong to two main serologic types, type I strains being obtained from 119 cases, and type II strains from fifty-seven cases. Strains obtained from cases occurring in members of the same family were found to be mainly of the same serologic type. Strains obtained from cases in small isolated outbreaks were found to be of the same serologic type.

AUTHOR'S SUMMARY.

ON THE IMMUNOLOGICAL NATURE OF THE PRINCIPLE IN SERUM RESPONSIBLE FOR THE WASSERMANN REACTION, WITH REFERENCE ALSO TO THE FLOCCULATION REACTION OF SACHS AND GEORGI. T. J. MACKIE and H. F. WATSON, *J. Hyg.* **25**:176, 1926.

An exhaustive study of the complement-fixation and flocculation reactions exhibited with the Wassermann antigens by the serums of certain normal, adult animals suggests that the related diagnostic reactions for syphilis may be occasioned by an abnormal increase of a "lipoidophile" antibody naturally present in the serum. The normal concentration of this antibody may be non-specifically augmented as a consequence of syphilitic infection in a manner analogous to the augmentation of natural antisheep hemolysin titer by heterogeneous stimuli.

ARTHUR LOCKE.

THE ANTIGENIC PROPERTIES OF EXTRACTS OF HORSE DANDER: III. SKIN REACTIONS AND PASSIVE TRANSFER OF HORSE DANDER SENSITIVENESS TO THE ANTIGENS OF HORSE DANDER EXTRACT. D. P. O'BRIEN, *J. Immunol.* **11**:271, 1926.

In the case of the patient (Reineke) whose asthma was caused by horse dander, the skin was highly sensitive to whole extracts of horse dander. It was likewise sensitive to the two protein fractions of the extract, differentiated by iso-electric precipitation. The skin of a normal person was found readily to be sensitized passively with the injection of serum from cases of hay-fever, rabbit asthma and horse asthma, so that the passively sensitized areas reacted twenty-four hours later to injections of extracts of ragweed and timothy, extracts of rabbit hair and extracts of horse dander. The passive sensitization of areas of the skin of a normal person by injection of serum from a patient whose asthma was caused by horse dander rendered these areas specifically sensitive to the two protein fractions of horse dander extract.

S. A. LEVINSON.

STUDIES IN ANAPHYLAXIS: IV. ALLERGIC MANIFESTATIONS IN FROGS. K. GOODNER, *J. Immunol.* **11**:335, 1926.

Frogs do not seem to show acute allergic manifestations as do mammals and it is suggested that this is due to certain peculiarities of physiology and innervation of the smooth muscle fibers. The excised sensitized frog heart is markedly affected on contact with the specific sensitizing substance, and this reaction seems to resemble light peripheral parasympathetic stimulation. It was shown that the muscle cells still respond to direct cellular stimulation. Excised smooth muscle from the alimentary tract of the frog did not exhibit the Schultz-Dale phenomenon and it is suggested that this may be explained by the fact that peripheral parasympathetic stimulation in this case does not produce contraction. These results would seem to offer further evidence that the precise site of the reaction is some portion of the neuromuscular complex. It would seem that the characteristic features of anaphylactic intoxication in different animals depends not alone on the distribution of nonstriated muscle but also on the character of the innervation of this muscle.

AUTHOR'S SUMMARY (S. A. LEVINSON).

STUDIES IN HYPERSENSITIVENESS: XX. A QUANTITATIVE STUDY OF THE INTERACTION OF ATOPIC REAGIN AND ATOPEN. P. LEVINE and A. F. COCA, J. Immunol. **11**:411, 1926.

The authors conclude that a quantitative study of the interaction between atopic reagin and its related atopen confirms the observation of Coca and Grove that the reagin is neutralized, that is, deprived of its sensitizing power by the admixture of the atopen, but that the activity of the latter is not lessened in any appreciable degree by the presence of its related reagin in the mixture. Confirming the observation of Coca and Grove, repeated reactions were obtained in the same sensitized site with the same concentration of the atopen. Such repeated reactions could be obtained even when the first "dose" of the atopen was mixed with the serum containing the reagin in vitro, that is, before its injection into the normal skin. The law of Coca and Kosakai regarding the fractional neutralization of precipitin applies in a modified form to the fractional "neutralization" of atopic reagin. After a passively sensitized skin site has been rendered insensitive, by repeated injections, to a certain concentration of the related atopen, a further reaction can be elicited with a stronger concentration, the ratio of the two concentrations being apparently constant with one atopic serum in the same skin.

S. A. LEVINSON.

STUDIES IN HYPERSENSITIVENESS: XXI. A QUANTITATIVE STUDY OF THE ATOPIC REAGIN IN HAY-FEVER. THE RELATION OF SKIN SENSITIVITY TO REAGIN CONTENT OF SERUM. P. LEVINE and A. F. COCA, J. Immunol. **11**:435, 1926.

The reagin content of serum of patients with early hay-fever examined by the authors was found to be practically proportional to the skin sensitivity. With the method of serum dilution, the A serums have about four times the sensitizing power of the B serums, which, in turn, have about four times the sensitizing power of the C serums. The ratios are distinctly greater with the method of atopen dilution. In two cases with disproportion of reagin content and skin sensitivity, there was a loss of reagins from the serum with no corresponding drop of skin sensitivity. In each case, this decrease of reagins was associated with a gradual decrease in severity of the symptoms. Quantitative study of the reagins in six cases of late hay-fever indicates that a similar proportion of reagin content and skin sensitivity exists in late hay-fever.

S. A. LEVINSON.

MUCOUS MEMBRANE IMMUNITY TO PNEUMOCOCCI IN RABBITS. MERLIN L. COOPER, J. Infect. Dis. **38**:491, 1926.

Rabbits die quickly of pneumococcus septicemia when type 1 pneumococci are introduced through a scratch in the buccal mucosa of the cheek.

Evidence is advanced showing that it is comparatively easy to stimulate the production of generalized immunity to the pneumococcus, type 1, in the rabbit by introducing a killed pneumococcus vaccine just beneath the buccal mucosa of the cheek.

A surprisingly small amount of vaccine is necessary for immunization, one minim on each of ten successive days being sufficient. A present this immunity has persisted for four months. All attempts to immunize subcutaneously and intradermally by injecting 1 minim on ten successive days, by instillation of 1 minim into the eye or by swabbing the nose and mouth have failed to result in any protective immunity.

AUTHOR'S SUMMARY.

STUDIES ON ANTHRAX IMMUNITY: 2. THE IMMUNIZATION OF SHEEP BY MEANS OF ANTHRAX BACILLI ATTENUATED WITH SODIUM CHLORIDE. S. J. SCHILLING, J. Infect. Dis. **38**:499, 1926.

A single injection of a sodium chloride attenuated culture of *Bacillus anthracis* protected sheep against subsequent infection with a virulent culture; the control animals died in fifty-four hours of typical anthrax. The immunity conferred by the vaccine was general. Vaccination and subsequent inoculation with virulent cultures were performed subcutaneously but in widely separated sites of administration.

Virulent anthrax bacilli may be found at foci of previous infection for some time following the apparent recovery of the infected animal.

The reduced pathogenicity as well as the antigenic properties of the sodium chloride attenuated culture of *Bacillus anthracis* appeared to remain fairly constant during cultivation on artificial medium.

AUTHOR'S SUMMARY.

HETEROLOGOUS CANCER GRAFTS: THE GROWTH OF MOUSE CANCER IN RATS. J. GHEORGHU, J. Path. & Bact. **29**:171, 1926.

Mouse carcinoma was transmitted to infant rats and rabbits under 24 hours old, and the tumor was maintained in the heterologous host through many serial passages, but after twenty passages in infant rats it was not possible to transmit the tumor successfully through adult rats. The specificity of the cancer for the homologous host, the mouse, was not lost during the passages. As the series progressed the onset of resorption became delayed and the process prolonged.

E. M. HALL.

AGGLUTINATION, CROSS-AGGLUTINATION, AND AGGLUTININ ABSORPTION IN TULAREMIA. EDWARD FRANCIS and ALICE EVANS, Pub. Health. Rep. **41**:1273, 1926.

On account of the frequent cross-agglutination between *Bacterium tularensis*, on the one hand, and *Bact. abortus* and *Bact. melitensis*, on the other hand, serums from suspected cases of tularemia and undulant fever should be tested for agglutination of tularensis and either abortus or melitensis, unless the clinical history points definitely to a recognized source of infection for tularemia or undulant fever.

A serum which shows a marked difference in titer for *Bact. tularensis*, on the one hand, and for *Bact. abortus* or *melitensis*, on the other, can usually be classed by the higher titer as due either to tularemia or to one of the varieties of *Brucella melitensis*.

A serum which agglutinates all three organisms to the same, or nearly the same, titer should be subjected to agglutinin absorption tests.

AUTHORS' CONCLUSION.

THE ISOLATION OF A CRYSTALLINE PROTEIN WITH TUBERCULIN ACTIVITY. FLORENCE B. SEIBERT, Science **63**:619, 1926.

The isolation of a crystalline protein with tuberculin activity is reported. The crystallized product elicits the characteristic skin reaction in tuberculous subjects. Chemically, it is shown that wherever the activity is lost, following enzyme treatment, there occurs also a corresponding reduction in whole protein, with an increase in proteose and residual nitrogen.

ENCEPHALOMYELITIS FOLLOWING VACCINATION. H. M. TURNBULL and J. MCINTOSH, Brit. J. Exper. Path. **7**:181, 1926.

Seven cases of encephalomyelitis following vaccination were studied. Contamination of lymph used did not seem to be of any significance as determined by examination, microscopic and cultural, of vaccination wounds. This encephalomyelitis belongs to the nonpurulent group, like poliomyelitis and epidemic encephalitis. Zones of softening around vessels in the white matter seem to be characteristic of all. The only virus demonstrated experimentally in the tissue of the brain and cord was vaccinal virus. In experiment this virus did not have neurotropic properties of exceptional intensity. Vaccinal encephalitis can be produced experimentally in animals.

S. A. LEVINSON.

THE TITRATION (STANDARDIZATION) OF TUBERCULIN. A. CALMETTE and DE POTTES, Ann. de l'Inst. Pasteur **40**:353, 1926.

A commission from the Committee of Hygiene of the League of Nations recommends as the most practical and reliable of the methods now used for the titration of tuberculin a series of intradermal inoculations in a sensitized guinea-pig, varying the amount of tuberculin and including a control with standard tuberculin. This method is superior to the complement-fixation titration, titration by flocculation, Koch's toxicity test and the cutaneous reaction in man. It measures the toxicity and antigenic value of several tuberculins in one animal, it is specific, and dispenses with unequal sensitivity of different animals. It is simple to interpret and comparatively rapid. The absolute value of a tuberculin (toxic and antigenic) must, however, be determined with the species of animal for which the tuberculin is intended.

G. B. RHODES.

THE PRODUCTION OF SPECIFIC ANTIBODIES BY EXPERIMENTAL INJECTIONS OF HYDATID FLUID. E. DUTTOT, P. CRAMPON and J. LEFEBVRE, Ann. de Parasitol. **4**:233, 1926.

There is a lack of unanimity as to the value of the complement-fixation reaction in the infection with *Taenia echinococcus*. The failure of the test in a number of instances is possibly due to the low antigenic value of the fluid obtained from echinococcus cysts and used in the tests. A standardized serum rich in echinococcus antibodies for the purpose of titrating the antigenic properties of hydatid fluid is therefore of a great practical importance.

The authors, by injecting intravenously sterile hydatid cyst fluid of a different origin in rabbits, have obtained a serum rich in hydatid antibodies. Their conclusions are as follows: 1. A repeated intravenous injection of hydatid fluid into rabbits leads to the appearance of specific antibodies detectable by the complement fixation reaction (by using fresh or heated serum).

2. Such a serum if sterile can be preserved in ampules.

3. The complement fixation reaction, for the detection of the echinococcus cyst in human beings, should be accompanied by a control reaction with the experimental standardized serum.

B. M. FRIED.

CONTRIBUTION TO THE STUDY OF ISO-AGGLUTININS. JEAN STAQUET, Arch. Internat. de Méd. Expér. **2**:71, 1926.

Of 1,072 Belgians (not more closely specified) 47.9 per cent belong to group 1 of Jansky's classification, 41.8 per cent to group 2, 7.1 per cent to group 3

and 3.2 per cent to group 4. This gives a racial index of 4.4 per cent according to the formula of L. and H. Hirschfeld. Two anomalous serums were encountered, one belonging to group 1 agglutinated certain corpuscles of that group, and the other belonging to group 2 agglutinated certain corpuscles of group 2 and of group 4. Because no agglutinin that is not present in one or the other parent ever is found in infants, it is emphasized that blood grouping may be of value in determining questions of paternity.

VACCINATION AGAINST DIPHTHERIA. P. LEREBoullet ET AL., Bull. et mém. Soc. méd. d. hôp. de Paris 50:683, 1926.

Lereboullet and his co-workers have vaccinated 1,414 children with diphtheria anatoxin. A dose of 0.5 cc. was given at the first injection, 1 cc. at the second and third, with three and one weeks intervals. Two injections induced immunity in 95 per cent; three in 100 per cent. The immunity still persisted up to eight and twelve months. Only in a little over 3 per cent of the cases, the children had to interrupt their usual occupations on account of vaccinal reactions. The elective age for immunization is between 2 and 3; the receptivity is then maximal, while the reactions are minimal.

ANATOXIN IN VACCINATION AGAINST DIPHTHERIA. FLANDIN, Bull. et mém. Soc. méd. d. hôp. de Paris 50:691, 1926.

Flandin injected 295 children with diphtheria anatoxin. There were no cases of diphtheria among the vaccinated within a year.

ORAL VACCINATION AGAINST CHOLERA. L. M. HOROWITZ-WLASSOWA and E. A. PIROJNİKOWA, Compt. rend. Soc. de biol. 94:1067, 1926.

The authors have tried: (1) to infect guinea-pigs by mouth with cholera; (2) to immunize them by the same way.

Since these laboratory animals are usually refractory to infection with the cholera vibrio they have resorted to Besredka's method of sensitization of the animals by giving them a preliminary dose of bile by mouth. As a result of their experiments, they have arrived at the following conclusions: 1. It is possible to reproduce by mouth a typical intestinal cholera in guinea-pigs, by using the Besredka bile sensitization method. 2. Guinea-pigs infected by this method with dead cholera vibrios become refractory to new infection by mouth (in certain instances guinea-pigs thus vaccinated acquire a general immunity). 3. Guinea-pigs vaccinated by mouth may acquire immunity against alimentary infection without showing traces of antibodies in their blood serum. In such instances the immunity is apparently purely cellular.

B. M. FRIED.

BLOOD GROUPS IN INFANTS. R. DEBRÉ and M. HAMBURGER, Compt. rend. Soc. de biol. 94:1196, 1926.

In fifty-six of eighty-seven cases did the blood group of the infant correspond to that of the mother. Examination for agglutinogens and agglutinins was made in fifteen cases. In two thirds of them the infant's blood corresponded to one of the four blood groups in adults. A total lack of agglutinins was noted in one third of the cases, a partial in one case. Their results correspond to those of Happ, and they disagree with Decastello and Sturli who believe that the appearance of agglutinins precedes that of agglutinogens.

IMMUNIZATION OF SCHOOL CHILDREN AGAINST DIPHTHERIA. HARVIER and RÉQUIN, Paris méd. 59:456, 1926.

Harvier and Réquin vaccinated with diphtheria anatoxin 228 school children with a positive Schick test. Two subcutaneous injections of 0.5 and 1 cc. were given, three weeks apart. Control Schick tests showed immunity in 95.4 per cent after two injections, and in 64 per cent after one injection. Pronounced reactions from the injections were never noted in children under the age of 7. Therefore, regular vaccination with diphtheria anatoxin may be made in all children between 2 and 7, without a preliminary Schick test. The latter appears positive in 78 per cent of children of this age. Two injections should be followed by a control Schick test. It is superfluous when three injections have been given.

ON THE SIGNIFICANCE OF THE PSEUDO- AND ANA-REACTIONS WITH DIPHTHERIA TOXIN. A. BACCICHETTI, Boll. d. Ist. sieroterap. Milan 5:145, 1926.

The pseudoreaction and the anatoxin reaction are both due to the hypersensitivity of the skin to the diphtheria proteins. Because heating the protein produces no change, the anatoxin reaction is more constant. The pseudoreaction varies with the individual, like the Pirquet test, depending on the skin sensitivity for intensity and duration, and has a bearing on the antitoxin response to vaccination. The Schick reaction is positive during the course of the disease, and quickly becomes negative after even small doses of antitoxin. A strong pseudoreaction indicates a favorable prognosis. In measles the pseudoreaction as well as the Schick reaction is unaffected. In some persons with a positive Pirquet reaction the pseudoreaction may last for years, while in others, especially in those vaccinated or those who have had diphtheria and received serum treatment, it disappears in a short time.

AUTHOR'S SUMMARY.

OBSERVATIONS ON COMPLEMENT FIXATION IN EXPERIMENTAL MYCOSIS (MYCOSIS FROM CANDIDA PINOYI, CASTELLANI). P. REDAELLI, Boll. d. Ist. sieroterap. Milan 5:157, 1926.

Serum from rabbits infected with *Candida pinoyi* (Castellani) or immunized with cultures killed with Lugol's solution, contains complement fixing properties, which aid in a general diagnosis of mycosis, and also give more specific reactions with the mold used than with molds of other families.

AUTHOR'S SUMMARY.

ANAPHYLAXIS TESTS WITH LIPOIDS. BRUNO POLETTINI, Boll. d. Ist. sieroterap. Milan 5:163, 1926.

Following the suggestions of the work by Sachs, Klopstock and Weil with lipid antibodies, mixtures of pure lecithin and cholesterol with swine serum were used in anaphylaxis experiments. In guinea-pigs only negative results were obtained with lecithin. With cholesterol, however, positive results were obtained in rabbits previously treated either with cholesterol alone or with cholesterol and serum, but with irregularities that indicate the need for further investigation.

AUTHOR'S SUMMARY.

SEROLOGY OF MOTHER AND FETUS. L. HIRSZFELD and ZBOROWSKI, *Klin. Wchnschr.* **5**:741, 1926.

Fetuses of the AB group (IV Jansky) are born from mothers of the O (I Jansky) group and fathers of the AB group less frequently than expected according to the laws of heredity. Perhaps a man of the pure formula AABB might not have any children at all with a woman of the group O.

A NEW ANTIGEN FOR THE SERO-DIAGNOSIS OF TUBERCULOSIS. C. NEUBERG and F. KLOPSTOCK, *Klin. Wchnschr.* **5**:1078, 1926.

The new antigen is an extract of dried tubercle bacilli with a 20 per cent solution of sodium benzoate.

ARTHUR LOCKE.

EXPERIMENTAL STUDIES ON SYPHILIS REINFECTION, IMMUNITY, ETC. H. REITER, *Klin. Wchnschr.* **5**:1356, 1926.

Syphilis reinfection produces only a subacute response, suggestive of partial immunity, except when the first infection has been quickly combated with active arsenic preparations.

ARTHUR LOCKE.

THE COMPLEX NATURE OF THE HUMAN BLOOD-GROUP SUBSTANCE. A. B. BRAHN and F. SCHIFF, *Klin. Wchnschr.* **5**:1455, 1926.

The residue from repeated alcohol and ether extraction of human erythrocytes is capable of binding the agglutinins of normal serum but gives no complement fixation with immune serum. A water extract of the alcohol extraction evaporation residue also binds the agglutinins of normal serum and may be dialysable. The alcohol-soluble fraction, freed from water-soluble and ether-soluble constituents, does not bind the agglutinins of normal serum but does give complement fixation with immune serum.

ARTHUR LOCKE.

INVESTIGATIONS ON THE ANTAGONISM OF PARASITIC INFECTIONS IN THE IMMUNITY PERIOD. A. JOSEPH, *Klin. Wchnschr.* **5**:1466, 1926.

The injection of related and antagonistic organisms (the trypanosomes of nagana) has no direct influence on resident parasites which remain from an earlier infection (of the spirochetes of relapsing fever).

ARTHUR LOCKE.

THE APPEARANCE OF ANAPHYLATOXIC PROPERTIES IN GUINEA-PIG SERUM ON LONG STORAGE. H. DOLD, *Klin. Wchnschr.* **5**:1472, 1926. THE APPEARANCE OF ANAPHYLATOXIC PROPERTIES IN SERUM ON SHAKING. *Ibid.*, p. 1281.

Sterile guinea-pig serum develops a turbidity on prolonged shaking or storage which may be the result of a denaturation process greatly accelerated at interfacial surfaces. The altered serum is anaphylatoxic to guinea-pigs.

ARTHUR LOCKE.

PRIMARY ALLERGY AND SHOCK. VON STARCK, *Monatschr. f. Kinderh.* **32**:119, 1926.

A boy, aged 1½ years, had eczema apparently due to peas. As the condition improved, the boy by way of a test was fed a soup containing peas and other vegetables, with the result that death occurred after he had swallowed three spoonfuls.

THE WASSERMANN AND FLOCCULATION REACTIONS IN SYPHILITIC MILK. P. HACKEMANN, München. med. Wchnschr. **73**:773, 1926.

The Berkefeld filtrates of the milk of syphilitic mothers give positive Wassermann, Sachs-Georgi and Meinicke reactions.

ARTHUR LOCKE.

THE DOSAGE OF EXPERIMENTAL TETANUS INFECTION AND ITS SIGNIFICANCE FOR SERUM THERAPY. A. WOLFF-EISNER, München. med. Wchnschr. **73**:1231, 1926.

The significance of the results in experimental tetanus is, in part, dependent on the accuracy of the dosage of tetanus organisms inoculated. A new and accurate method of infection is proposed in which a titrated, fine suspension of earth and tetanus bacilli is injected into a fold of the skin.

ARTHUR LOCKE.

FUNDAMENTAL REMARKS ON DIPHThERIA, DIPHThERIA ANTITOXIN CONTENT OF THE BLOOD (TISSUE) AND ACTIVE DIPHThERIA PROTECTIVE INOCULATION. H. DOLD, München. Med. Wchnschr. **73**:1271, 1926.

Prophylactic immunization against diphtheria is not undertaken for the purpose of producing a definite antitoxin concentration in the blood or tissues. The aim is to produce a great responsiveness in antitoxin production as a protection against subsequent diphtheritic infection.

ARTHUR LOCKE.

LIPOMA OF THE STOMACH. W. SPITZMÜLLER, Wien. klin. Wchnschr. **39**:538, 1926.

A submucous lipoma of the stomach, 20 cm. long and 27 cm. in circumference, is described. There were two ulcers in the mucous membrane over the tumor, and the patient had suffered from pains of increasing severity for six months before the removal of the growth.

EXPERIMENTAL STUDIES OF PRECIPITIN AND SPECIFIC CUTI-REACTION: II. ON THE APPEARANCE OF PRECIPITIN IN PREVIOUSLY IMMUNIZED ANIMALS. G. SHOJI, Acta derm.-venereol. **7**:425, 1926.

In rabbits, after a second injection (0.1 cc.) of egg white or human, horse or sheep serum, following the disappearance of precipitins produced in the blood serum by the first injection, the reappearance of precipitin is the same after cutaneous or intravenous administration, usually in about seventy-two hours, with a maximal in from ninety-six to 120 hours. The persistence of the precipitin tends to become longer after many injections.

ETHEL B. PERRY.

EXPERIMENTAL STUDIES OF PRECIPITIN AND SPECIFIC CUTI-REACTION: II. THE DISAPPEARANCE OF INJECTED ANTIGEN IN THE BLOOD OF NORMAL AND IMMUNIZED ANIMALS RESPECTIVELY. G. SHOJI, Acta derm.-venereol. **7**:541, 1926.

After intravenous injections the duration of antigen (human, horse and sheep serum) in the circulation tends to shorten as the precipitin titer rises, but in rabbits in which the precipitin response decreases with repeated injections the antigen remains in the blood perhaps even longer than in the normal animal. After previously induced precipitins have disappeared from the serum, injected antigen disappears quickly, long before precipitins reappear.

After intracutaneous injections (0.1 cc.) less antigen appears in the blood than with intravenous injections, and the highest content is found in about forty-eight hours. The Arthus reaction increases with the precipitin titer, and the antigen appearance becomes fainter. If the serum titer does not increase, the antigen appears more readily in the blood after each injection. The conclusion is that the cutaneous tissue of the immunized rabbit gains ability to "throw off" to some degree the reinjected antigen, and antigen which does appear in the blood may be eliminated more rapidly by the immunized than by the normal animal.

ON THE APPLICABILITY OF THE COMPLEMENT FIXATION REACTION IN URINARY TUBERCULOSIS: PART I. ON THE INFLUENCE OF URINE ON THE HEMOLYTIC SYSTEM IN THE COMPLEMENT FIXATION REACTION. MEGUMI TAKAHATA, *Tohoku J. Exper. Med.* 7:293, 1926.

From work with sixty-five specimens from normal persons and 126 from patients with different diseases conclusions were made that inhibition of hemolysis in complement-fixation reactions with urines was no indication of the type of sickness, and depended on several factors, including especially the specific gravity, the amount of urine used in the test and the acidity. The best procedure seemed to be with from 0.1 to 0.2 cc. amounts, with neutralization of the urine if indicated.

Tumors

SERIAL TRANSMISSION OF CHICKEN TUMORS BY MEANS OF INJECTIONS OF LEUKOCYTES AND PLASMA. M. R. LEWIS and H. B. ANDERVONT, *Am. J. Hyg.* 6: 498, 1926.

Two tumors, the Rous sarcoma and the Carrel indol tumor, were passed from chicken to chicken by means of the blood. Either the plasma or the washed leukocytes of a chicken that had a well developed tumor were employed for transmission. In a few instances a transplant from a tumor, previously produced by means of the blood, was utilized. Every transplant, even though taken from a tumor after several passages by way of the blood, resulted in a tumor in both the Carrel and the Rous series. These tumors developed more rapidly than did those obtained from the injections of the blood. So far, there has been a higher percentage of tumors from the injection of leukocytes than of plasma.

LIPOMA OF THE BROAD LIGAMENT WITH A REPORT OF A CASE. R. M. RAWLS, *Am. J. Obst. & Gynec.* 11:305, 1926.

Rawls reports a lipoma occurring in the left broad ligament of a negress, aged 37, who had never been pregnant. She complained of gradual enlargement of the abdomen associated with pain and swelling in the left foot. The mass was easily shelled out except for its lower pole which was intimately connected with the deep pelvic and femoral vessels. Microscopic examination showed the tumor mass to consist of large fat cells surrounded by thin interlobular connective tissue septums. The ten true lipomas reported in the literature have varied in size from a few cubic millimeters to a large tumor mass reported by Middelschute, weighing 33 pounds (15 Kg.). They occurred in women between the ages of 31 to 64. The only symptoms were those of pressure in tumors of large size.

A. J. KOBAK.

HYPERNEPHROMATA. A. BOTHE, *Ann. Surg.* **84**:57, 1926.

In a human embryo of 16 mm., the anlage cells of the suprarenal cortex are in close proximity to the metanephric cells. This he considers evidence in favor of the theory that hypernephromas arise from suprarenal rests in the kidney. In one case, suprarenal rest tissue was found adjacent to an actively proliferating hypernephroma. Chemical analysis of hypernephroma tissue conforms closely to that of suprarenal tissue and he has experimentally produced slight hyperglycemia following injection of extract of the tumor. The literature on the subject is summarized, and twenty-two cases are presented with a discussion of their morphologic features.

N. ENZER.

ENDOTHELIAL MYELOMA, EWING. CHARLES L. CONNOR, *Arch. Surg.* **12**:789, 1926.

Sixty-seven cases of Ewing's tumor, in this paper designated endothelial myeloma, have been recorded in the Registry of Bone Sarcoma of the American College of Surgeons. This constitutes about 10 per cent of all the bone tumors registered, and they are considered important enough clinically and pathologically for report in full. The belief that these form an entity separable from osteogenic sarcoma is borne out by the characteristics here emphasized; namely, their almost constant location in the shafts of the long bones and in flat bones where osteogenic sarcoma seldom occurs, their peculiar morphology, the type of cell being easily distinguished from the osteoblast in most cases, and their susceptibility to radium and roentgen-ray treatment. The cells do not form an intercellular substance that will stain with the dyes used to differentiate collagen, bone and cartilage. At the same time the cells are separable from those arising from the primitive hemocytoblast, and are considered therefore to be different from other various forms of myeloma which presumably arise from that cell. They resemble other myelomas by their predilection to metastize to other bones.

They occur in children mainly, and many of them are preceded by trauma and by signs of inflammation, apparently resulting from the trauma, this inflammation reaction passing so imperceptibly into malignant disease that the two seem inextricably associated in the early stage.

Histologically they may be divided into angiomatous, reticular and diffuse, the first perhaps somewhat less malignant, being furthest differentiated, the last the most malignant. The reticular type is considered the parent type, the other two being variations of this caused by location and differences in rate of growth. Several tumors studied were seen to arise apparently from the reticulum of the bone; this observation, with the evidence presented concerning the embryologic development of the reticular cell from a primitive mesenchyme cell, seems to indicate that the origin is in the cells of the reticulo-endothelium of the bone marrow. Because it is desired to express this origin in the name, the tumor has been called endothelia myeloma, thus sharply distinguishing it from all other bone and bone marrow tumors.

Several important characteristics almost constantly associated with the tumor are the slow development with intermittent pain, swelling that may recede only to return and to become progressive and the distressingly frequent confusion with chronic osteomyelitis clinically, roentgenologically and even occasionally histologically. But diagnosis is possible in most cases by correlation of the history and physical signs with a rather typical roentgenographic picture. As a final distinguishing point, the therapeutic radium or roentgen-ray test is advocated, this tumor, in contrast to osteogenic sarcoma, usually melting away, under the influence of these forces.

Contrary to the opinions of Ewing and others, it is thought that endothelial myeloma arises as a solitary tumor, the multiple tumors appearing as actual metastases, and for this reason it is believed that amputation in the early stage is a form of treatment to be considered, though cure has been obtained in several cases, apparently, by radium.

The prognosis, with a combination of surgery and irradiation, is not always death. Patients have lived for five years or longer (one for sixteen years) after amputation, and many who have been treated by a combination of surgery, radium, the roentgen ray and Coley's toxins, are living over three years after the onset of the disease. The prognosis seems distinctly better than that of osteogenic sarcoma and other myelomas, and for this reason it is urged that these be considered special cases in which, by energetic measures, a permanent cure may be possible.

AUTHOR'S SUMMARY.

MALIGNANT EPITHELIAL NEOPLASMS, CARCINOMA AND EPITHELIOMA, OCCURRING IN PERSONS UNDER TWENTY-SIX YEARS OF AGE. L. HAYNES FOWLER, Surg. Gynec. Obst. **43**:73, 1926.

Carcinomas and epitheliomas are usually considered to be tumors of middle or later life. Fowler studied and analyzed 112 cases of pathologically demonstrated carcinoma and epithelioma in patients under 26 years of age, on whom operations were performed at the Mayo Clinic between 1914 and 1924. The youngest patient in this series was 1 year old, and of the entire group sixty-five were females and forty-seven males. Clinically this group of cases was characterized by a relatively short history; symptoms of moderate severity but rapid progress; definite physical observations; from moderate to marked loss of weight in most cases; little anemia, and a high mortality. The total known mortality was more than 50 per cent (18.7 per cent could not be traced). Only 14.2 per cent were alive more than three years after operation. Carcinoma and epithelioma are found in practically every organ of the body, in youth. They are most frequent in the large intestine. In Fowler's series there were fourteen cases of carcinoma of the rectum and an equal number of ovarian carcinomas. The other organs involved were: the stomach in nine cases; the thyroid, breast and kidneys each in seven cases; the testicle, lip and cervix, each in five cases, and miscellaneous organs in thirty-nine cases. In the thyroid the carcinoma is usually intracapsular in an adenoma, and is found by the pathologist and not the surgeon. The pathologic condition of the neoplasms varied in the different organs. The cells vary in degrees of differentiation. The large undifferentiated cells with large oval or round nuclei and deeply staining nucleoli predominated. The lack of hyalinization, fibrosis, lymphocytic infiltration and cellular differentiation may be responsible for the greater malignancy of neoplasms in the young.

M. L. PARKER.

THE SERUM DIAGNOSIS OF CANCER. THE PHENOMENON OF REDUCTION. C. MONDAIN, R. DOWRIS and J. BECK, Ann. de l'Inst. Pasteur **40**:431, 1926.

In this study of the Thomas-Benetti reaction the authors conclude that serums from cancerous patients do not reduce methylene blue in the presence of extracts of cancer tissue more actively than do serums from normal persons. They find the process is due to micro-organisms which are present primarily as spores in the tissue extract.

G. B. RHODES.

SERODIAGNOSIS OF CANCER. H. HARTMANN, Bull. Acad. de méd., Paris **95**:412, 1926.

Hartmann describes an improved technic for the Botelho seroreaction in malignant disease. The protein content of the serum has to be brought to a standard figure, 7 or 8 per cent. Then 0.5 cc. of the serum is mixed with 3 cc. of a 1 per cent solution of nitric acid in 0.75 per cent sodium chloride solution. On the light foam which forms on agitation, he drips 0.5 cc. of a solution of 1 Gm. of iodine and 2 Gm. of potassium iodide in 210 Gm. of water. The test is negative if the content remains clear; positive, if it becomes turbid. In 145 patients with cancer the reaction was positive in 90.4 per cent; in fifty-five patients with other diseases it was negative in 85.5 per cent. The reaction was positive in women in the first months of pregnancy. In seventeen subjects operated on for cancer, the reaction remained positive in twelve, and the cancer recurred in all in this group. In five, the test became negative after the intervention, and recurrence was observed in only one. The reaction became negative in six of twenty-one patients with cancer after roentgen-ray or radium therapy; all appeared clinically cured. In fifteen, the reaction continued positive, and all except one developed recurrences. The reaction was positive in all the rabbits with tar cancer and it was negative in normal animals except in one gravid rabbit.

HEREDITARY HEMORRHAGIC ANGIOMATOSIS. P. EMILE-WEIL, Bull. et mém. Soc. méd. d. hôp. de Paris **50**:1135, 1926.

A woman, aged 36, presented, besides progressive obesity, numerous angiomas, developing within the last six years. The angiomas, about thirty in number, the size of a large pin head, were located on the face and lips. Six small angiomas were on the tongue, and a few bright red spots on the body. There were also varices of the legs. Bleeding from the nose was frequent. Similar lesions occurred in the mother, a sister, a brother and an aunt. A grandfather suffered from recurring epistaxis. A woman, aged 43, presented similar phenomena. Angiomas or hemorrhages occurred in a grandfather, father, brother, two sisters, an uncle and a cousin. In both patients, the bleeding time was normal, coagulation retarded.

SYSTEMIC PRIMARY SPINDLE-CELL SARCOMA OF THE LYMPH GLANDS. E. GIOJA, Haematologica **7**:201, 1926.

Almost all the lymph glands had become transformed into sarcomatous tissue in a man, aged 62. The first manifestation of the disease had been a small tumor at the upper part of the right thigh. It had been six months in developing and finally ulcerated. The whole lymphatic system gradually became involved, including the tonsils. Necropsy revealed this and the fact that the disease had spread to adjoining organs and to the skin, possibly by retrograde invasion of the lymphatics. No infectious process is known that produces the histologic picture of spindle-cell sarcoma, and no form of cancer is known that presents the features of this case and the two similar ones on record. There were no special blood changes and no fever, but the bone marrow showed a predominance of young hemohistioblasts.

Four colored plates accompany the article.

The patient died from intercurrent septicemia in two years.

E. CUSHING.

SPINDLE CELL SARCOMA OF CORVINA. A. H. ROFFO, Bol. d. Inst. de med. exper. **3**:206, 1926.

Of 125 fish with tumors, caught at Mar del Plata in 1925, 90 per cent of the neoplasms were in the region of the mouth. Two tumors in the scaly part are described. Histologically they were composed of spindle cell.

THE TOXICITY OF TUMORS AND ITS RELATION TO THE PROTEINS. A. H. ROFFO and R. LOPEZ RAMIREZ, Bol. d. Inst. de med. exper. **3**:216, 1926.

The toxic action of extracts of tumors from the white rat, like that of extracts of normal tissues, seems to depend on the protein content and the molecular integrity of these proteins.

ETHEL B. PERRY.

THE RELATION $\frac{\text{POTASSIUM}}{\text{CALCIUM}}$ IN NEOPLASTIC TISSUE. A. H. ROFFO and J. LASERRE, Bol. d. Inst. de med. exper. **3**:221, 1926.

During the early period of development when the rate is faster, the quotient $\frac{\text{Potassium}}{\text{Calcium}}$ is higher than at any other times and seems dependant on changes in the potassium since the calcium remains nearly constant. This condition is the same as in embryonic tissue.

ETHEL B. PERRY.

GANGLIONEUROBLASTOMA OF BRAIN. F. PAUL, Beitr. z. path. Anat. u. z. allg. Pathol. **75**:221, 1926.

To the interesting group of tumors which contain proliferated ganglion cells or their precursors, Paul adds a tumor of the cerebellum of a boy, aged $5\frac{3}{4}$ years. It was an actively growing neoplasm, histologically malignant, and was composed of immature ganglion cells, glia, nonmedullated nerve fibers, and neuroblasts. Tumors of the ganglioneuroma and neuroblastoma types, arising usually from the sympathetic system or its derivatives, constitute an important group of neoplasms, the neuroblastomatous ones especially in children. Those originating within the central nervous system are rare, unless, as appears probable, many of the cerebral tumors usually described as malignant gliomas are neuroblastomas. Of tumors of the central nervous system which contained ganglion cells, Paul could find eight recorded. He accepts the name ganglioglioblastoma for tumors like his own.

O. T. SCHULTZ.

EXPERIMENTS WITH EXPLANTED ROUS SARCOMA. F. WIND, Klin. Wchnschr. **5**:1355, 1926.

The Rous sarcoma may grow temporarily under anaerobic conditions. It is more capable of anaerobiosis than is a yeast culture, providing glucose is not excluded.

ARTHUR LOCKE.

DIAGNOSIS OF MALIGNANT TUMORS OF THE KIDNEY. S. L. EHRLICH and M. M. FRISCHMANN, Virchows Arch. f. path. Anat. **259**:565, 1926.

The authors conclude that the small, wormlike clots in the urine which Israel described as pathognomonic of malignant renal tumors have no great diagnostic value. They place greater reliance on the presence in the urine of hematoidin crystals, degenerated cells of epithelial type and bits of tissue.

O. T. SCHULTZ.

PRIMARY CARCINOMA OF THE OVIDUCT. Z. LIANG, *Virchows Arch. f. path. Anat.* **259**:577, 1926.

Two cases of primary carcinoma of the fallopian tube are reported and the data relating to 214 previously reported cases are summarized. The tumor is papillary in character and may have multiple points of origin in the mucosa. It grows along and through the mucosa, transforming this into tumor tissue which contains pseudo-alveoli but no true glandular spaces. The tubal carcinoma manifests its malignancy earlier than other papillomatous neoplasms. The tumor penetrates the wall, metastasis occurring by implantation and by the lymph stream, more rarely by the blood stream.

O. T. SCHULTZ.

TERATOMA OF BRAIN. G. L. DERMAN, *Virchows Arch. f. path. Anat.* **259**:767, 1926.

In a teratoma of the brain of a month-old child, Derman found epithelium of various types, cuboidal, cylindric, pigmented and squamous. Cartilage, bone and striated muscle were also present.

O. T. SCHULTZ.

TUMORS OF THE KIDNEY. J. OBERZIMMER, *Virchows Arch. f. path. Anat.* **260**:176, 1926.

Of sixty-three tumors of the kidney, fifteen were embryonal mixed tumors, seven carcinomas, thirty-six hypernephromas and five tumors of the pelvis of the kidney. The carcinomas and the hypernephromas, the latter being termed hypernephroid tumors, were selected for more detailed study. The carcinomas are glandular tumors of the kidney which fall into three groups, tubular, solid alveolar, and papillary or cystic papillary. Oberzimmer claims that the hypernephroid tumors are of the same three types, that their cellular peculiarity is the result of secretory activity with retention of secretion within the cells, and that the tumors are not derived from suprarenal tissue but are nephrogenic in origin.

O. T. SCHULTZ.

RHABDOMYOMA OF VOLUNTARY MUSCULATURE. A. ABRIKOSSOFF, *Virchows Arch. f. path. Anat.* **260**:215, 1926.

Rhabdomyoma of voluntary musculature is probably the rarest of all neoplasms. Abrikossoff reports five, three of the tongue, one of the upper lip and one of the muscles of the calf of the leg. The clinical data are meager. One of the tumors of the tongue recurred. In addition to striated cells, large round cells were present which were incompletely or not at all striated. Abrikossoff believes that rhabdomyomas develop from myoblasts which have been formed in the regenerative process following injury to striped muscle. He thinks that many of the tumors originating in voluntary muscle and termed sarcomas are probably sarcomatous forms of myoblast tumors.

O. T. SCHULTZ.

EPENDYMAL TUMOR OF BRAIN. E. SILBERBERG, *Virchows Arch. f. path. Anat.* **260**:251, 1926.

Silberberg reports a tumor of the roof of the fourth ventricle in a boy, aged 10 years. It was partly cystic, and was composed of cells of epithelial type like those of the lining ependyma of the ventricles; the cells were often

arranged about small glandlike spaces. No neurofibrils or glia fibrils could be detected. The author considers the tumor a neuro-epithelioma derived from the ependyma. He believes that such tumors should be included under the neuroblastomas.

O. T. SCHULTZ.

GENERALIZED SARCOMATOSIS IN A HEN. J. MICHALKA, Virchows Arch. f. path. Anat. **260**:399, 1926.

A condition of generalized sarcomatosis in a hen was believed to have originated as a small round-cell sarcoma of the ovary.

O. T. SCHULTZ.

THYROID TUMORS IN COLD-BLOODED ANIMALS. F. W. MÜLLER, Virchows Arch. f. path. Anat. **260**:405, 1926.

Müller reports a benign parenchymatous and cystic colloid goiter in a snake, *Zonurus giganteus*, and a carcinoma of the thyroid in a fish of the carp family, *Jordanella florida*. He devotes considerable discussion to the similarity of his fish tumor to the thyroid enlargements of trout; he concludes that iodine deficiency is probably an important factor in thyroid enlargements and tumors of lower animals, but that species disposition is also active, since the condition occurs so much more frequently in some species than in others.

O. T. SCHULTZ.

TWO CASES OF SARCOMA OF THE HEART. F. WOHLGREN, Svenska Läk.-Sällsk. Handl. **52**:12, 1926.

Case 1.—The patient was a woman, aged 53, who began rather suddenly to have chills and fever, but there was no leukocytosis and no growth in cultures of the blood. The heart was enlarged to the left; there was no increase of blood pressure. Cough with bloody expectorate set in and also symptoms of multiple cerebral embolism. Death occurred about six months after the onset of the illness. There was a walnut-sized, spindle cell sarcoma with hemorrhages and necrosis of the medial and anterior wall of the right auricle with infiltration all through the pericardium which was adherent, and numerous small metastatic nodules in the lung, liver and brain.

Case 2.—A man, aged 57, had "catarrh of the lungs" with bloody expectorate. Roentgen-ray examination showed changes in the lungs and mediastinum that were regarded as metastases. Necropsy revealed a spindle cell sarcoma of the wall of the right auricle that nearly filled the cavity of the auricle and invaded the right lung; numerous scattered metastases were found in both lungs.

Medicolegal Pathology

TRANSFIXION [ACCIDENTAL] OF THE MEDULLA OBLONGATA BY A DARNING NEEDLE; WITH REGARD TO THE MEDICAL AND MEDICOLEGAL ASPECTS. C. V. WELLER, Ann. Clin. Med. **3**:107, 1924.

If a complete necropsy had not been performed, the cause of death would not have been found. A needle, 59 mm. long, with its entire surface oxidized, was found completely perforating the medulla oblongata near the midline, with the point protruding 3 mm. anteriorly and the eye embedded in the ligamentum nuchae. There was little hemorrhage and no inflammatory reaction, and the traumatic necrosis about the perforation was funnel shaped, possibly from

movements of the head while the needle remained fixed. There were polymorphonuclear cells in the tissues about the puncture of the skin. Death occurred about four hours after the probable accident. No other condition was found that might have caused death, which, it was concluded, resulted from an accidental puncture probably accomplished by a backward fall. The body was lying partly on the floor with the arms and head thrown back over a cot. A needle left in a cushion or blanket, overturned to bring the point up, would have been held by the buckram cover of the cot, according to the tests made, with enough resistance for the puncture. The conclusion received support not only from the circumstances but also from the character of the victim. The needle was like one found in the stocking she had been darning; she was known to leave needles stuck carelessly in chairs and cushions; and there was nothing to suggest a suicidal tendency. Homicide was out of the question, as was also insertion of the needle after death.

E. B. PERRY.

HOMICIDAL GUNSHOT WOUNDS OF THE HEAD IN UNUSUAL LOCALIZATIONS.
RUGGERO ROMANESE, *Arch. di antrop. crim.* 46:26, 1926.

The horizontal path of the bullet through the temple is an argument against the theory that suicide was committed. A further argument in one of the four puzzling cases related was that the track of the bicycle had been straight and even until it swerved abruptly at the point where the body was found with a bullet through the right temple, the revolver being found close by. The absence of powder marks and the fact that it was the left temple excluded suicide in another case. In a third case, the entering point of the bullet was merely a little farther back than the customary suicide wound. The horizontal bullet wound was in the mouth in one case, the lips being intact; it was in the same location in a fifth case in which the bullet had been discharged accidentally from a distance of several feet. It had entered at the junction of the hard and soft palate, and the small opening might easily have been overlooked. In the other case the bullet had entered the upper jaw from outside the teeth.

DISPLACEMENT INTO BLOOD VESSELS AND EMBOLISM DURING LIFE OF TISSUE FROM THE CENTRAL NERVOUS SYSTEM; SIMILAR DISPLACEMENT POST MORTEM.
H. MERKEL, *Deutsche Ztschr. f. d. ges. gerichtl. Med.* 7:217, 1926.

With the report by Abrikossoff in 1913 of this form of "parenchyma-cell embolism" a new variety was given a place with the other more familiar forms in which cells from the placenta, liver or bone marrow serve as emboli and are carried by the blood to adventitious locations, principally the lungs. In Abrikossoff's case due to buttock presentation and laceration of the transverse sinus of the dura of a new-born infant, embolism of tissue identified as from the cortex of the cerebellum occurred into the left coronary artery. Of course, the foramen ovale was still open and served as part of the course taken by the embolus. In Merkel's case observed in the body of a man who fell from a ladder, the embolism was into the upper lobe of each lung and the masses of brain tissue (also from the cerebellum and torn by external violence) were grossly visible.

Merkel also found a displacement of brain tissue into the jugular veins and their tributary veins due to development of gas and other postmortem changes in the body of a woman found in the water. There was no injury of the head. In the consideration of adipocere in the tenth edition of Hofmann's work on

legal medicine, revised by Haberda [vol. 2, p. 977], mention is made of a similar condition found by Hofmann. The material which he compared to "coagulated fat" had extended down the neck veins into the heart.

E. R. LeCOUNT.

BULLET WOUND OF THE CHEST. MURDER OR SUICIDE. K. WALCHER, *Deutsche Ztschr. f. d. ges. gerichtl. Med.* 7:301, 1926.

Local officials who first examined the body thought that a poacher had been shot from behind by one of his companions because the wound of the front of the chest was much the larger. Subsequent and more careful examinations demonstrated that the rifle had been placed with the muzzle against the clothes covering the chest, that the splinters of fractured ribs were carried dorsally and that powder blown all the way through the chest had blackened the inside of the broken seventh rib at the exit wound, but not its outer surface. The large size of the entrance wound in front on the left side was due to several layers of clothing there being shot against the skin and into the chest. The three poachers, caught by some hunters, had barricaded themselves in a hut; the two survivors stated that when the shot was fired they had seen no flame and supposed, because of the muffled sound, that the shot was outside. From the direction of the 7.9 mm. caliber bullet through the chest, and its location in a beam of the building, it was decided that the deceased had leaned over the muzzle, while standing, and pushed the trigger with his thumb.

E. R. LeCOUNT.

A CASE OF DEATH FROM AN OVERDOSE OF AMIDOPYRINE. KORBEN GEILL, *Deutsche Ztschr. f. d. ges. gerichtl. Med.* 7:344, 1926.

A girl, aged 22, took an unknown quantity of amidopyrine. She was attended by a police surgeon, who found her unconscious, with the pupils widely dilated. The girl had several convulsions, and then her pulse became imperceptible. An injection of caffeine was given, the stomach was emptied, and a soapy, foamy, fluid obtained. A postmortem investigation revealed nothing characteristic. The brain was highly vascular and moist, and the convolutions were flattened. The tongue contained several wounds, which appeared like tongue-bites; the surrounding tissue was filled with blood. The lungs on the cut surface were bloody; a foamy fluid was scraped off. The heart was slightly enlarged, blood clots were found in the heart chambers, and the myocardium was brown-red, slightly anemic and firm. Hemorrhages were noted in the left ventricle. The liver was large, vascular, soft and mottled. The spleen was large, vascular, firm and bloody on the cut surface. The stomach was contracted, the mucosa being swollen and somewhat loosened, and contained 100 cc. of gray-brown turbid fluid, having the odor of fermented raspberry juice.

A chemical analysis of one fourth of the examined organs revealed that they contained 0.746 Gm. of amidopyrine or 3 Gm. of amidopyrine in 4 Kg.

Relatives stated that the patient was in the habit of taking amidopyrine to relieve headache.

Rotky in Prague (*Wien. Arch. f. inn. Med.* 10:595, 1925) reports that a woman, aged 36, in the course of one night, took 7 Gm. of amidopyrine for the relief of neuralgia. The next morning the patient was highly excited. The stomach was washed out twice, and milk and soap suds were given to produce vomiting; 2 Gm. of amidopyrine were recovered in the vomitus. The patient's pulse was so rapid that it could not be counted; the temperature was sub-

normal, 35.3 C.; tremors throughout the body; the reflexes were increased; there was tenesmus of the urinary bladder; she was anxious and conscious all the time. The next day she felt better, but every ten minutes, a dark red urine was voided which gave a red precipitate with ferric chloride. On the second morning she had fever and rigidity, but no longer frequency of urination; there was a measles-like eruption on the face spreading to the neck and shoulders, and the buccal and pharyngeal mucous membranes. The reflexes remained exaggerated for one week. On the fourteenth day the last attack of muscle rigidity, clenched teeth and increased reflexes occurred. Recovery occurred gradually, but there were always unforeseen rises in temperature; this condition lasted for weeks so that convalescence progressed slowly.

W. D. McNALLY.

POSTMORTEM HANGING IN AN ATTEMPT TO HIDE MURDER. A. WERKGARTNER, *Deutsche Ztschr. f. d. ges. gerichtl. Med.* 7:424, 1926.

It was only by a narrow margin that murder was finally detected when, enamored of another woman, a husband strangled his wife and then hanged the body in an attempt to duplicate the conditions of suicidal hanging. Because of his ill repute and comments the wife had made to neighbors of her fear of being poisoned, a postmortem examination was made, and fractures of the coid and left horn of the thyroid cartilages were found. The body was not entirely suspended by the husband after death, but left hanging in a semi-sitting position, the noose about the neck such as persons committing suicide do not use.

Some time after the crime, the husband confessed and described what he had done in detail; but before this happened, those who made the medical investigation were compelled to insist repeatedly that the conditions found by them were totally inconsistent with suicide.

EXPERIENCE IN HAMBURG IN THE POSTMORTEM EXAMINATION OF NEW-BORN INFANTS. W. BORCHERS, *Deutsche Ztschr. f. d. ges. gerichtl. Med.* 8:5, 1926.

Forty-seven of the ninety-two bodies examined during six years were live-born; sixty-six were of unknown parentage, and ten born in and sixteen out of wedlock. Seventeen were murdered, eight by strangulation, four by throttling and two by asphyxiation with foreign material, such as paper stuffed into the throat. Of the twenty-eight bodies found in the water, seven were so decomposed that question of live or still birth and of violence were not answerable. Thirteen of these twenty-eight were born dead, eight were murdered.

Murder was more common with those born illegitimately. No mention is made of methods to determine whether the child breathed after birth, except seeing whether the lung tissue floated in water.

THE IMPORTANCE OF EXTRA-UTERINE PREGNANCY IN LEGAL MEDICINE. E. FUCHS, *Deutsche Ztschr. f. d. ges. gerichtl. Med.* 8:50, 1926.

Extra-uterine pregnancy is tubal in from 91 to 95 per cent of the cases; consequently, in the two of twenty considered by Fuchs in which there were some reasons for regarding the pregnancy as ovarian, a higher ratio than usual prevailed.

Rupture with death from hemorrhage may follow unusual exertions and has been known to occur following physical conflicts between husband and wife.

The legal status of the husband under such circumstances is largely concerned with his cognizance of the pregnancy.

Since rupture is frequently attended by cramps of the abdomen and vomiting, finding death due to hemorrhage in the abdomen from the broken gestation sac frequently results in removal of the suspicion of poisoning. The rupture may be brought about by attempts to produce abortion; this occurs in both married and unmarried women. Inability to bring on the abortion by methods generally employed successfully is sometimes followed by more violent attempts that bring on death without serious interference with the pregnancy outside the uterus.

Tubal pregnancy usually is followed by spontaneous rupture of the sac between the second and third months of pregnancy, and death usually results in a few hours from internal hemorrhage, unless surgical relief is obtained.

SUDDEN DEATH FROM NATURAL CAUSES. H. KOOPMANN, *Deutsche Ztschr. f. d. ges. gerichtl. Med.* 8:91, 1926.

That 502 of the 839 deaths were due to heart disease, with aortic syphilis playing a large part, is in accord with other similar reviews. Profuse and fatal hemorrhage from tuberculosis caused twenty-seven of the 187 deaths grouped under disease of the lungs; apoplexy is represented by only forty-seven deaths.

It is remarkable how frequently in incidence are included studies of sudden spontaneous death such as this, and deaths from alcohol and from suffocation due to inhalation of foreign bodies. Koopmann mentions nine of the former and thirty-four of the latter; and their inclusion destroys the value of his numerous carefully calculated percentages, so far as they apply to deaths solely from natural causes. Some other and more obvious cause for death was present in all but five of the 142 bodies with well marked status thymico lymphaticus. Presumably histologic studies were made in efforts to explain the sixteen deaths not accounted for, four of them with this lymphatic constitution, but mention of such examinations is omitted.

Reference has been made to the frequency of syphilis of the aorta with deaths from heart disease. In the 150 bodies in which chronic leptomeningitis was found, the cause for death was heart disease for 105, and alcohol for twenty others. No explanation is offered for the leptomeningitis, and the question of its syphilitic origin is not raised.

The blood in the heart cavities was fluid in 229 of the 472 bodies in which its state was noted, but discussion of the importance of this is unaccompanied by information regarding the time after death these particular examinations were made. Claims made by others for frequency of fibrous pleuritis in the bodies of persons dying unexpectedly were not supported, although with deaths from apoplexy and pneumonia, its incidence was higher than the average.

THE RELATION OF STATUS LYMPHATICUS TO LEGAL MEDICINE. E. KRUGER, *Deutsche Ztschr. f. d. ges. gerichtl. Med.* 8:116, 1926.

The lymphatic constitution is gradually losing the importance it has held for so long. This tendency was given considerable impetus by so frequently finding in the bodies of young adults killed during the war the overgrowth of lymphoid tissues by which the lymphatic constitution is characterized. When it is present, there is commonly other evidence of a development incomplete or abnormal in other ways. The suggestion has been made that the anomaly has associated with it, lessened ability to develop properly supporting framework of organs, this is accompanied by an increase in cellular lymphoid elements.

The importance of this condition for legal medicine is two-fold. Its presence offers an opportunity for differences of opinion to develop; presumably it will henceforth, as in the past, hinder the thorough search for the cause for death which should be made in postmortem examinations, and which would be made if the lymphatic constitution were not present.

In children the enlarged thymus may cause death mechanically by pressure; in adults, however, this does not occur. Its relation to deaths which occur in the water without drowning, to sudden deaths by accident and to suicide is doubtful.

The suicide, as well as the lymphatic constitution in the individual who commits suicide, are both to be regarded as anomalous manifestations, but without any causal relationship.

By some the claim has been made that hyperthymisation is associated with a defective function by the suprarenal glands, and that shock of various kinds or chloroform inhalation is followed by an outpouring of epinephrine into the blood, which quickly exhausts the supply and death results. Some of the results of removal of all or a part of the enlarged thymus seem to support this contention.

Kruger mentions having access to records of 141 cases of status thymico-lymphaticus. He has a table of the ages, from 6 months to 57 years, for thirty-two persons, with the weight of the enlarged thymus. He fails to discuss the amount of adipose tissue in such enlarged glands or the degree to which it had replaced the lymphoid tissue. He mentions finding eosinophils abundantly in the gland. The focal or disseminated acute interstitial myocarditis reported by Fahr and others, he failed to find in the hearts he examined microscopically. The deaths of the thirty-two persons were mainly suicidal, and by hanging or drowning.

THE POSTMORTEM EXAMINATION OF EXHUMED BODIES. H. SCHMEISSER, *Deutsche Ztschr. f. d. ges. gerichtl. Med.* 8:162, 1926.

Because of the general use in America of embalming, the expediency of postmortem examination of exhumed bodies is well recognized. In Europe, however, embalming is not a common practice and the desirability of such examinations has long been discussed.

It is interesting to learn that at Hamburg from 1900 to 1925, in the 2,591 necropsies for medicolegal purposes, only nine were of exhumed bodies and all but two were examined in the latter half of this period. Schmeisser reviews the advantages of such examinations, citing instances resulting in removal of suspicion from innocent persons and others in which conviction of the guilty followed uncovering of crime. When issues are concerned with fractures or bullet wounds of bones exhumation is definitely indicated, even though the body has been buried a long time. Other conditions, such as pneumonia, apoplexy, pregnancy, abortion, fat embolism, glottis edema and suffocation with inhaled vomitus may be found, and live or still birth may be determined.

As yet no satisfactory explanation has been made of the unforeseen and startling preservation of histologic detail sometimes encountered in organs and other structures removed for microscopic study from unembalmed exhumed bodies. The degree of humidity and other characteristics of the soil in which the body has been buried, obesity or its absence, the cause of death, and the loss of considerable blood before death are among the important factors influencing postmortem decomposition.

Technical

A METHOD OF OBTAINING VAGINAL SECRETION FOR BACTERIOLOGICAL EXAMINATION WITHOUT THE POSSIBILITY OF VULVAL CONTAMINATION. J. W. HARRIS and J. BROWN, *Am. J. Obst. & Gynec.* **11**:497, 1926.

A double glass tube instrument for obtaining vaginal secretion uncontaminated by the flora of the vulva or region of the introitus was devised. The inner tube is fitted snugly into an outer, the former measuring 220 cm. and the latter 120 cm. in length. A rubber cylinder is cuffed over the outer tube and invaginated into the end of the inner tube, sealing the opening of both tubes at one end. This is assembled with a swab within the inner tube and sterilized. The instrument is inserted into the labia, and the inner tube is pushed piston-like through the outer, unfolding the rubber cylinder and allowing the swab to come in contact with the upper vaginal vault. The efficiency of this instrument has been tested by smearing *Bacillus prodigiosus* over the labia of ten women liberally, but vaginal material collected in these cases was free from the red colonies of this organism.

A. J. KOBAC.

THE TECHNIQUE OF THE RED CELL SEDIMENTATION REACTION. A. WESTERGEN, *Am. Rev. Tuberc.* **14**:94, 1926.

The technic of the reaction, as recommended by the author, is discussed in detail as in previous publications.

MAX PINNER.

A SIMPLIFIED METHOD FOR DETERMINATION OF THE SPECIFIC GRAVITY OF A FEW DROPS OF URINE. JOHN KIRKPATRICK and DAVID H. KLING, *J. A. M. A.* **87**:487, 1926.

In a urometer jar, in the proportion of 1:3.5, carbon tetrachloride and xylene, respectively, are placed; for example, 10 cc. of the former and 35 cc. of the latter. They are mixed thoroughly by stirring. The resultant specific gravity will be 1.020 at 77 F. For each degree change of temperature below this standard, one must add to the urometer reading 0.0005 degree and, vice versa, if above this reading, one must subtract 0.0005 degree. That is, for each 2 degrees change in temperature, the standard urometer scale changes 0.001 degree.

A drop of urine is let fall into this mixture. If the drop sinks to the bottom, it must be higher in specific gravity than the mixture. Therefore, the specific gravity of the mixture must be changed to equilibrium by adding carbon tetrachloride, drop by drop, slowly with adequate stirring, until the drop of urine will have a distinct tendency neither to rise nor to fall. This indicates equilibrium of the mixture. The reading on the urometer scale will be equivalent to the specific gravity of the urine, after necessary correction for temperature difference has been made. If the drop of urine floats, the specific gravity of the mixture may be depressed by the opposite procedure of adding xylene in small amounts, until the drop of urine has a distinct tendency neither to rise nor to fall. Correct results depend entirely on adequate stirring of the mixture and temperature corrections.

The mixture may be used repeatedly. However, it is best to filter off the urine after its specific gravity has been determined.

THE COMPARISON OF THE ELECTROMETRIC AND COLORIMETRIC METHODS FOR DETERMINATION OF THE p_H OF GASTRIC CONTENTS. G. KAHN and J. STOKES, *J. Biol. Chem.* **69**:75, 1926.

The colorimetric method is not sufficiently accurate for the determination of the p_H of gastric contents which are less acid than p_H 2.1. Above p_H 2.1, dialysis of the specimen against physiologic sodium chloride solution and the colorimetric estimation of the p_H on the dialysate are essential for even moderate accuracy. The electrometric method should be used when considerable accuracy is required, guarding against loss of carbon dioxide whenever the p_H exceeds 5.5.

AUTHORS' SUMMARY.

A STUDY OF THE NEW BENEDICT METHOD FOR THE DETERMINATION OF BLOOD SUGAR. R. ROCKWOOD, *J. Biol. Chem.* **69**:187, 1926.

The new Benedict method for blood sugar was compared to the Folin-Wu method in a series of 300 samples of blood. The Benedict reagents which have been used to date do not require as great a correction for lack of proportion in color development as the Folin-Wu reagents. The normal cases in this group show a mode between from 75 to 85 mg. per hundred cubic centimeters and a range of from 50 to 120 mg. The difference value between the Folin-Wu and Benedict methods does not seem to be correlated with any factor in the condition of the diabetic patients. The cuprous oxide precipitate in the Benedict test is more difficulty soluble than in the Folin-Wu test, especially with high blood sugars. The substance causing the difference value is apparently not one of the ordinary nitrogenous reducing substances since the difference value is not increased in uremia. Sugar tolerance tests show no characteristic variation in the difference value. The substance causing the difference value seems to be present in greater quantity in the cells than in the plasma and is sometimes only present there.

AUTHOR'S SUMMARY.

A DISTINCTIVE TEST FOR CYSTEINE. M. X. SULLIVAN, *Pub. Health Rep.* **41**:1030, 1926.

In the unmodified test using a 0.5 per cent solution of naphthoquinone-4-sodium sulphonate, followed by sodium hydroxide, many substances gave a brownish color. If, however, after ten minutes a 2 per cent solution of freshly prepared sodium thiosulphate, in half normal sodium hydroxide is added, cysteine alone retains the red. Cystine, reduced with sodium cyanide, and hydrolyzed glutathione yield cysteine and so give positive reactions, while reduced glutathione does not react but does give a positive nitroprusside test and so may be distinguished. The interference of such substances as pyrogallol, phloroglucinol and pyrrol, the only ones of the eighty compounds tested that did interfere, can be obviated by the sodium sulphite modification and sodium cyanide reduction, so the test appears to be highly specific for cysteine.

ETHEL B. PERRY.

PRESERVATION OF BLOOD. C. TOSCANO, *Policlinico* **33**:545, 1926.

The addition of a little sodium fluoride preserves blood for from four to six days without interfering with the test (Bang) for sugar.

COMPARATIVE STUDIES ON THE PRODUCTION BY RABBITS OF PRECIPITATING ANTISERUM FOR PROTEIN DIFFERENTIATION. DICKOFF, *Centralbl. f. Bakteriol.* **99**:478, 1926.

The juice is expressed after frozen meat has been thawed rapidly and subdivided. After centrifugalization or filtration, about 2 cc. of the fluid is injected intravenously into rabbits. Rabbits which have a fever above 40 C. after this injection are tested on the ninth day, and bled, if the precipitin titer of the serum is 10,000 when tested with the corresponding serum. Rabbits which do not show any rise of temperature, after the injection of muscle juice, are said to be poor precipitin producers. Reinjection may be performed after five days with double the original amount of antigen, and later, if necessary, with three times that amount.

MODIFICATION AND IMPROVEMENT OF THE BECHER-HERRMANN MICRO-METHOD FOR THE DETERMINATION OF BLOOD SUGAR. E. KAUFMANN, *München. med. Wchnschr.* **73**:771, 19296.

Light-fast dye solutions are substituted for the unstable color standards in the Becher-Herrmann micro-method for the determination of blood sugar.

ARTHUR LOCKE.

A SIMPLIFICATION OF THE QUANTITATIVE DETERMINATION OF IODINE IN THE URINE IN THE POTASSIUM IODIDE KIDNEY FUNCTION TEST. A. NARATH, *München. med. Wchnschr.* **73**:1066, 1926.

The iodine determination is carried out on a potassium nitrate fusion of an evaporation residue of the alkalinized urine. After acidification of the solution of this fusion mixture (through the interaction of the nitrous and hydriodic acids released), the contained iodine is extracted with chloroform and determined colorimetrically.

ARTHUR LOCKE.

VITAL STAINING OF AMYLOID. HELENE HERZENBERG, *Virchows Arch. f. path. Anat.* **260**:466, 1926.

Previous work by the author had confirmed the statement of Bennhold that amyloid can be vitally stained by Congo red and had shown that trypan blue is an equally selective vital stain for amyloid. This led her to try other vital dyes in mice with experimental *Staphylococcus amyloidosis*. Of the acid dyes tried in this series of experiments, Congo red and trypan blue caused good staining of the amyloid. By the sixteenth day after the injection the stain had disappeared completely from the material. Trypan red and lithium carmine caused slight staining, and pyrrol blue and indigo carmine did not stain the amyloid. The basic dyes tried, toluidin blue and neutral red, were poorly borne by the animals. Since the two dyes which stain amyloid vitally are acid, the author concludes that amyloid has a basic character.

O. T. SCHULTZ.

STAINING REACTIONS OF CORPORA AMYLACEA. W. SCHMIDT, *Virchows Arch. f. Anat.* **260**:474, 1926.

Although the corpora amylacea of the prostate, lung and spinal cord gave the iodine and methyl violet reactions of amyloid, the effect of the action of chemicals which influence the staining reactions of true amyloid was variable in the case of corpora amylacea.

O. T. SCHULTZ.

Society Transactions

CHICAGO PATHOLOGICAL SOCIETY

Regular Monthly Meeting, Nov. 8, 1926

LLOYD ARNOLD, M.D., *President, in the Chair*

THE NORMAL BACTERICIDAL MECHANISM OF THE GASTRO-INTESTINAL TRACT. PRESIDENTIAL ADDRESS BY DR. LLOYD ARNOLD.

Some of the results of this study can be summarized briefly as follows:

By operative procedures certain segments of the small intestine are fixed to the anterior abdominal wall in such a way that material can be obtained for study.

The normal reaction of the content of the duodenum and upper part of the jejunum is slightly acid (p_H from 5.2 to 6.5). When this reaction is made alkaline, there is a change from the usual obligate bacterial flora to a fecal type. The normal hydrogen-ion concentration of the content of the duodenum and jejunum seems to depend to a great extent on the normal gastric secretion.

Some of the nutritional disturbances have been explained on the basis of this bactericidal property of the upper part of the small intestine. Moro's endogenous infections in infants were given particular attention, and the beneficial results that have followed the ingestion of protein milk, buttermilk, lactic acid milk, hydrochloric acid milk and all such acid buffered foods are regarded as influencing to a great extent the duodenal function of the infant.

Bacteria introduced into the dog's stomach with alkaline buffered milk reach the cecum in large numbers during a relatively long period. When the same bacteria are given by mouth in acid buffered milk, they sometimes reach the cecum, but in small numbers, and during a relatively short period. Bacteria introduced into the stomach in an acid buffered aqueous solution seldom reach the cecum. When suspended in alkaline buffered aqueous solution, the bacteria reach the cecum in almost the same concentration as the original ingested suspension. Perhaps the "auto-disinfecting" mechanism of the upper part of the small intestine is dependent on acid buffered material. This reaction is insured in the healthy animal by the normal gastric secretion. When neutral or alkaline buffered material enters the duodenum, the bactericidal power is lost and the bacterial content of such material reaches the cecum.

As a result of a statistical study of the diarrheal death rate in infants under 5 years of age in New York city, it seems that one of the probable factors in the increased resistance of young infants to diarrhea is the extensive use of acid buffered foods during the last decade, as suggested by Finkelstein and others.

Some evidence has been presented to show that mice are rendered more susceptible to infection by mouth of certain paratyphoid bacteria when fed on a diet that contains a relative large amount of alkaline buffered material. Mice fed on a diet that contained much less alkaline buffered substances have a greater resistance to the same dose of the bacteria.

It seems from these results that the normal bactericidal mechanism of the gastro-intestinal tract plays a major rôle in the susceptibility or resistance (nonspecific) of the host to certain enteric infectious diseases.

MESENTERIC CYST OF THE JEJUNUM. DR. BERNARD PORTIS. (From the Nelson Morris Memorial Institute for Medical Research and the Surgical Department of the Michael Reese Hospital, Chicago.)

Cysts of the mesentery of the small intestine are comparatively rare and still less frequently produce clinical symptoms. The cyst of the jejunum described here caused intestinal obstruction. There were several other congenital abnormalities.

Cystic tumors of the peritoneum may be lymphatic or chylous, enteric or urogenital, or they may be dermoids and teratoids.

The chylous cysts are large, single or multilocular tumors, or numerous small swellings of the mesentery, omentum, intestinal wall or retroperitoneal region. They contain clear fluid, chyle or inspissated fatty material, and often blood. The walls are fibrous tissue with many round cells or lymph follicles and often dilated lymph spaces. Smooth muscle tissue may be present as in enteric cysts, and there may be a lining endothelium. Giant cells may form about the fatty detritus.

The enteric cysts are either single or multiple, large or small, usually along the lower ileum, in the wall of the intestine at the place of a Meckel's diverticulum, in the mesentery or near the navel. When originating within the muscular wall of the intestine they remain attached to the convex side or project into the mesentery. They contain mucilaginous, colorless, yellow or brown fluid. The wall resembles that of the intestine and may contain smooth muscle, mucosa, crypts, lymphoid tissue and a lining of cylindric, cuboidal or stratified epithelium, sometimes papillary.

The urogenital cysts are large, single, multiple or multilocular and involve the mesentery and adjacent organs or extend into the pelvis. They occur chiefly in adult women, and contain brown serous fluid with pseudomucin. The wall is fibrous tissue with a cylindric or cuboidal epithelial lining, and there may be suprarenal cortex or tissue resembling embryonal kidney.

The dermoid cysts are rare.

Report of Case.—A girl, aged 5½ years, entered the Michael Reese Hospital on Aug. 11, 1926, service of Dr. Julius Hess, with abdominal pain of eight weeks' duration, loss of weight and appetite, and constipation. The abdominal pain, located just below the navel, frequently severe, and cramplike in character, usually occurred after eating and continued for from fifteen minutes to several hours. Loss of appetite, weight and strength followed, constipation was marked and vomiting occurred several times.

The essential changes, physically, concern the distended and resistant abdomen. A cystic tender tumor mass was palpated in the lower right quadrant. Peristalsis was not noted at first, but on the following day some was noted in the upper right quadrant. The von Pirquet and Mantou tuberculin tests gave negative reactions. Among the diagnoses considered were tuberculous peritonitis, Meckel's diverticulitis and atypical appendicitis.

Roentgen-ray examination of the chest and abdomen did not disclose any changes excepting an abnormal fixation of the cecum and ascending colon in the liver region, with an irregularity of the cecum that suggested a tumor.

There was a mild secondary anemia; the leukocytes numbered 11,200, the urine contained acetone but not albumin, and the feces did not contain blood.

The child, when seen again on August 17, had symptoms of intestinal obstruction, and an operation was advised. With local anesthesia a right pararectal incision was made, and a tense cystic tumor mass was found. Ethylene anesthesia was then given because of the tumor size. The incision was enlarged,

and the tumor mass, about 10 by 8 by 6 cm., was removed from the abdomen. It lay in the mesentery of the jejunum, the jejunum in front like a taenia coli. The intestine on the cyst was almost collapsed. The bowel was resected proximal and distal to the tumor, and the ends closed and inverted. The tumor was then amputated at its mesenteric attachment, care being taken not to interfere with the blood supply. In removing the tumor, one of the cysts was opened and a yellow gray, odorless fluid escaped. The two ends of the intestine were united by a lateral anastomosis and the mesentery was sutured so as to prevent pocket formation.

The report from the pathologic laboratory revealed the following: In a piece of small intestine, between the folds of the attached mesentery, were four, fluid containing, communicating cysts, from 2 to 4 cm. in diameter. Another large cyst which had been opened was 5 by 4 cm. The wall was about 1 mm. thick. The inner surface was corrugated by branching strands of yellow gray tissue. The cysts were all close to the bowel. The outer surface of the cyst was dark red. The cyst wall was composed of fibrous tissue with small bundles of smooth muscle widely separated. There was no recognizable cellular lining. In the wall were a number of dilated lymphatics. The outer portion of the cyst wall was directly continuous with the connective tissue of the outer surface of the intestine. The pathologic diagnosis was "lymphogenous cyst of the mesentery."

The condition of the patient was improved after the operation. Cereals were given the following day. However, attacks of vomiting appeared, the child growing rapidly worse, and death occurred the third day after the operation.

An abstract of the conditions found at necropsy, which was done by Dr. Norbert Enzer, follows: "The abdomen is rounded and has a recent operative wound about 8 cm. in length in the lower right rectus region.

"The pleural and pericardial cavities, the lungs, and the heart are without noteworthy changes.

"The omentum covers the bowel completely. There is a generalized acute fibrinous peritonitis. Most of the small bowel is distended with gas and dusky red but nowhere necrotic. The lateral anastomosis of the two loops of the jejunum from which the mesenteric cyst has been removed is intact, 30 cm. from the pylorus. The stomach is normal; the pylorus is tightly contracted in rigor mortis. The duodenum and the first part of the jejunum are markedly distended. About 15 cm. from the pylorus the bowel passes posteriorly through an opening in the mesentery into an infraduodenal fossa on the left of the spine, beyond which it proceeds upward for a short distance, then to the right and back again through the same opening in the mesentery. This portion of herniated jejunum is markedly distended and dusky red. The hernial sac is a thin membrane resembling mesentery. The herniated loop of bowel is 10 cm. long. About 6 cm. below the hernia and lying just in front of it is the anastomosis. In this region the bowel is distended and discolored, though less marked until about 20 cm. from the cecum; there a second discolored and slightly cyanotic loop of bowel is caught in the same hernial ring."

RIEDEL'S STRUMA OF THE THYROID. DR. O. T. SCHULTZ.

Since Riedel in 1896 described a fibrous tissue replacement of the thyroid gland, some forty-five instances of this relatively rare thyroid disease have been reported. Clinically, the thyroid is moderately enlarged, hard and fixed

to the surrounding tissues, changes which usually have led to the preoperative diagnosis of malignancy. The surface may be smooth or slightly nodular. The capsule is thickened, and the thyroid tissue is pale, firm and with little colloid.

Among 305 thyroid glands surgically removed at the Michael Reese Hospital since 1917, Riedel's struma was observed three times, two being received in the pathologic laboratory within one month of each other during the present year, and one during the latter part of last year. The three were from women, of the ages 26 and 46 years, respectively. In all, pulse, temperature and respiration were normal. None had exophthalmos, although in two the clinical diagnosis was toxic goiter; in the third, carcinoma. The basal metabolic rate was minus 5 per cent in the first, plus 29 to 34 per cent in the second with repeated tests, and minus 20 per cent in the patient supposed to have carcinoma. In all, the thyroid gland was slightly enlarged, the increase having appeared gradually within from two to six months.

In the youngest of the three patients, whose basal metabolic rate was minus 5 per cent, the thyroid had not been completely transformed into the hard, ligneous tissue present in the other two thyroid glands. In the latter, the follicles were compressed by a large amount of moderately cellular, interfollicular connective tissue, and richly infiltrated by lymphocytes and plasma cells. The follicular epithelium is high and frequently surrounds a small amount of deeply stained inspissated colloid. In many follicles both colloid and lumen have disappeared, the epithelium forming a multinucleated syncytial mass. In a few follicles less compressed by the ingrowth of connective tissue, the epithelium is low and the lumen filled with deeply stained colloid.

The clinical recognition of the nature of the condition is important, since the usual diagnosis of malignant growth leads to an unnecessary operation, sometimes followed by immediate mortality or by laryngeal paralysis, the latter accident having occurred in this series in the case diagnosed clinically as carcinoma.

The change apparently is a nonspecific granulomatous inflammation, in which thyroid hyperplasia and inflammation of the upper respiratory tract have no part. In the three cases presented nothing could be found corresponding to the remnants of the postbranchial body described by Louise Meeker, whose presence she suggests may be a factor in the transmission of an inflammatory process from the pharynx to the thyroid.

Regular Monthly Meeting, Dec. 13, 1926

LLOYD ARNOLD, M.D., *President, in the Chair*

RHABDOMYOMA OF THE TONGUE. KAETHE DEWEY.

The complete report will be published in the ARCHIVES.

ANTERO-MEDIAN MERO-ACRANIA (NOSENCEPHALOS) WITH HYPOGASTROSCHISIS DEXTRA AND MALFORMATION OF THE FINGERS AND TOES. ERNST PRIBRAM.

A demonstration was given of a fetus with the anomalies mentioned. The nomenclature was discussed. The time during gestation when the malformations began and the cause were considered. A complete report will be published in the ARCHIVES.

BILIARY TRACT PROTOZOIASIS. FRANK SMITHIES.

In 1917, my interest in biliary tract protozoiasis was aroused by finding viable *Lambli*a *intestinalis* (Stiles, 1902) or *Giardia intestinalis* in the bile of a gallbladder removed by Dr. A. J. Ochsner. It seems that this was the first observation of *Giardia* in the human gallbladder, and it was reported before the American Gastro-Enterological Association in May, 1920 (Proceedings: discussion of report by John C. Hemmeter).

Since 1917, gallbladder and bile tract fluids have been examined on a warm stage of the microscope, in hanging drop or slide preparations, for further instances of protozoan infestation; and since 1921, search has been made for protozoa and other intestinal parasites, in material secured by the duodenal tube, during bile tract drainage, according to the Lyon method or its modifications.

This report concerns thirty-three instances in which protozoa were demonstrated in bile-containing fluids secured from the duodenum after stimulation of the mucosa by a warm 33 per cent water solution of magnesium sulphate. It was not possible, in any instance, to obtain from the duodenum, material containing protozoa, prior to the introduction of magnesium sulphate solutions.

The identification of the protozoa is given in the *Medical Clinics of North America*, 1917. The fresh warm material is examined on the heated stage of a microscope. Encysted forms of the parasite should be noted carefully, especially when endamebae are present. Mixed infestations are not uncommon. Sometimes the parasites are demonstrated by the first examination, but they may be found only after several trials.

In the thirty-three patients, protozoa were found as follows: *Chilomastix mesn*eli, 23; *Endamoeba histolytica*, 11; *Endamoeba coli*, 1; *Trichomonas intestinalis*, 4; *Giardia (lamblia) intestinalis*, 2.

Single infestations were: *Chilomastix mesn*eli, 18; *Endamoeba histolytica*, 5; *Giardia intestinalis*, 2, and *Trichomonas intestinalis*, 1; while concomitant infestations were: *Chilomastix* and *Endamoeba histolytica*, 4; *Trichomonas* and *Endamoeba histolytica*, 1; *Trichomonas* and *Endamoeba coli*, 1; and *Trichomonas*, *Chilomastix* and *Endamoeba histolytica*, 1.

The thirty-three infestations were found during the examination of 1,591 patients, an incidence of 2 per cent. A recent study of alimentary tract protozoiasis in 3,780 patients demonstrated parasites in 265, or 7 per cent. It seems likely that the careful examination of duodenal fluids for protozoa will demonstrate a greater incidence than this report mentions.

Seventeen patients had lived in or visited southern states or countries; sixteen lived in rural sections of Ohio, Illinois, Idaho and Kansas, of which eleven had travelled in subtropical or tropical regions, and of these four had bloody diarrhea while abroad. People who live in the North and who visit tropical or subtropical regions appear more susceptible to bile tract protozoiasis than do those who have always lived in southern regions and who may be chronic protozoa carriers.

In this series, there were sixteen females and seventeen males, the youngest patient a boy of 8 years and the oldest a woman of 66.

In twenty-nine, cysts or vegetative forms of protozoa were found in the stools—cysts more often. When protozoa were found, some biliary tract inflammation was present.

A surgical removal of the gallbladder was performed in eight patients in whose duodenal fluids protozoa were found. In the contained fluids protozoa were demonstrated, of the kind found in the duodenal fluid. These protozoa were *Endamoebae histolytica*, 6; *Chilomastix*, 1; *Giardia*, 1. In five instances

Chilomastix was associated with *Endamoeba histolytica* and in one patient *Trichomonas* with *Endamoeba histolytica*. In two gallbladders there was empyema; in two, stones, and in four, catarrhal cholecystitis with regions of edema and ulceration. Acute changes were noted especially in the gallbladder of a *Chilomastix* carrier.

When vegetative forms of *Endamoeba histolytica* infest the bile tracts, lesions similar to those in the bowel may be expected. If cysts only occur, the host may be a harmful carrier. The cysts may be discharged from the biliary tract, and give rise to vegetative forms in the bowel that cause ulcers. It is not possible to enumerate the changes caused by the presence of the flagellates in the bile tracts, but removing them seems beneficial to the patient. The gallbladder and bile passages as local foci for reinfection should not be overlooked.

ADENOMA OF THE PARATHYROID. CHESTER C. GUY.

A woman, aged 29, with a tumor of the neck for six years, had symptoms of pressure from a growth that seemed to be in the left lobe of the thyroid. This mass was removed at the Cook County Hospital. The tumor was 8 by 6 by 4 cm., encapsulated, and had a cortex of soft, yellow lobulated tissue, and a medulla of necrotic, partly calcified tissue. Microscopically the cortex contained epithelial cells resembling those of the parathyroid. The diagnosis was adenoma of the parathyroid.

The patient returned ten months later with three nodular swellings in the neck in the position of other parathyroid glands. These were thought to be a compensatory hyperplasia rather than metastases of the tumor which was removed.

DISCUSSION

DR. H. JAFFÉ: The diagnosis of a parathyroid tumor should be made with extreme caution. Parathyroid hormone can be demonstrated in mice with a suitable extract of the tumor.

PATHOLOGICAL SOCIETY OF PHILADELPHIA

Regular Meeting, Dec. 9, 1926

EUGENE L. OPIE, *Presiding*

AORTIC ANEURYSM WITH ASSOCIATED INVAGINATION OF CAROTID ARTERY. R. S. GRAHAM.

The specimen (shown in the figure) was removed from a colored man, aged 40, at the Pennsylvania Hospital. The heart and aorta were removed together, and the left common carotid artery could not be found, although the dissection was carried up into the neck to the level of the cricoid cartilage. Evidences of syphilitic aortitis were manifest in the ascending and transverse portions of the arch. A large saccular aneurysm approximately 10 by 10 by 8 cm. arose from the transverse aortic arch, compressing and partially eroding the wall of the left bronchus.

The lumen of the aorta was of about normal size. Below and posterior to the innominate artery the orifice of the saccular aneurysm, measuring 5 by 2.5 cm., opened into the thick walled sac which contained clotted blood. Just to the left of the innominate artery, at the usual site of the left common

carotid, a tubular structure resembling an artery projected into the aortic lumen for a distance of about 1.5 cm. On the adventitial surface of the aorta, opposite this structure, was a depression covered with loose fibrous tissue. Careful dissection here revealed a strand of fibrous tissue extending down into the structure within the aorta, and it was possible to pass a small probe through its lumen. With some manipulation it was also possible to evert this structure, so that it then appeared like the stump of a normal artery, terminating abruptly at a point 1.5 cm. distal to the arch.

Microscopically, in cross section, this invaginated structure shows the histologic architecture of an artery, but the intimal layer, with a well defined internal elastic membrane, is seen at the periphery, and the tissue lining the lumen appears to be identical in character with adventitial tissue.

Several factors which have contributed to the formation of this unusual lesion are unexplained. That the carotid artery should be represented by a short, sharply truncated stump, associated with the apparent absence of the



The transverse arch of the aorta, with lumen exposed, showing invaginated stump of carotid artery projecting into the lumen.

distal portion of the artery, would seem to be due either to a developmental defect, or to an atresia resulting from thrombosis or some other cause. The arterial stump had evidently invaginated into the aortic lumen, reversing the order of the coats by this process, causing the lumen to become lined by adventitia, and the periphery by intima. It is again difficult to explain what factors could have caused this inversion, as one would naturally suspect that the effect of the blood pressure would have been exactly the opposite.

Similar examples of this unique puzzling lesion have not been found in the literature.

HEALED BACTERIAL ENDOCARDITIS. EDWARD WEISS.

Two specimens were demonstrated showing extensive calcified lesions of the aortic and mitral valves. Their appearance suggested previous bacterial endocarditis with healing. One patient, a colored man, aged 53, had had symptoms of cardiac decompensation for one year; the other, a white man, aged 52, had not had any cardiac disease which was recognized during life. The healing of bacterial endocarditis, as here exemplified, is believed to be rare.

A CASE OF TUBERCULOSIS IN WHICH THE LESION IS CONFINED TO THE PLEURA,
PERICARDIUM AND MYOCARDIUM. B. L. CRAWFORD.

This case is of interest in showing advanced tuberculosis of the heart, without demonstrable pulmonary lesions. The patient was a colored woman, aged 29, who was admitted to the Philadelphia General Hospital with symptoms of cardiac decompensation, pericarditis and pulmonary tuberculosis, though definite signs of tuberculosis of the lung could not be elicited by physical examination.

At autopsy both pleural cavities were found to be obliterated by dense adhesions, except at the right base, where a small pocket containing clear fluid was found. The right pleura was markedly thickened especially at the base, where it measured 1 cm. in thickness. The pericardial cavity also was obliterated by adhesions and the pericardium thickened. The heart was slightly enlarged and the cavities were dilated, but there was not any lesion of the valves. There were several firm, circumscribed, grayish yellow nodules in the wall of the right auricle. The nodules protruded into the cavity of the auricle. The largest one measured 2.5 cm. in thickness. Both lungs were atelectatic, but gross evidence of tuberculosis could not be found. The peribronchial lymph nodes were not enlarged, but several of the mediastinal nodes were enlarged and caseous. Amyloid infiltration was present in the liver and spleen.

LESIONS IN THE PULMONARY ARTERY IN RHEUMATISM. JOHN R. PAUL.

The available pathologic material of the cases of acute rheumatism at the Pennsylvania Hospital has been reviewed recently, and from the necropsy series of the last twenty-five years, eighteen cases, all of which showed typical Aschoff bodies in the myocardium, were selected for study. Tissue from the aorta was available in only a small number, but in general sections have shown the lesions described above. In one case I was fortunate in finding tissue from the base of the pulmonary artery, and it is through the work of Dr. Longcope, who performed the autopsy twenty years ago, that the material was made available.

A white man, aged 32, was admitted to the hospital in November, 1906, showing evidences of extreme cardiac decompensation. He had suffered from the initial attack of rheumatic fever at the age of 9 and probably had had another attack at the age of 23. He died about a week after admission. At necropsy the typical pancarditis of rheumatism with accompanying severe cardiac decompensation was observed. Grossly the pulmonary artery showed a macroscopic lesion which was described as "moderate sclerosis."

In the sections of the myocardium there were many beautiful Aschoff bodies. Typical Aschoff bodies were also found in the adventitia of the base of the aorta and pulmonary artery; the lesion being more pronounced in the latter. The medial coat of the pulmonary artery was the seat of an extensive destructive lesion. Isolated, partially hyalinized, circular areas, rich in elastic tissue, survived here and there, separated by scar tissue marking the site of the distal or outer half of the medial coat, with adjacent evidences of slight proliferative endarteritis. The marked similarity which these areas in the mediums bore to the contiguous adventitial Aschoff bodies in size and shape was noteworthy, although the cellular structure was quite different. In general, the lesion was similar to those which have been described in the aorta but it was unique in its extent and in its location in the pulmonary artery.

RHEUMATIC DISEASE OF THE HEART. WILLIAM C. VON GLAHN.

Study has been made of a series comprising 109 cases of rheumatic disease of the heart, in which autopsies were performed at the Presbyterian Hospital, New York city, over a period of twenty years. Histologic data have been collected, especially from seventy-four cases since 1920. Histologic changes in the endocardium, myocardium and pericardium were discussed, with special attention to the structure, derivation and significance of the Aschoff nodule.

Analysis of the 109 cases reveals interesting facts. Forty-eight patients (44 per cent) were males and sixty-one (56 per cent), females. The distribution of lesions in the heart is shown in table 1.

TABLE 1.—*Distribution of Lesions in the Heart*

Valves	Acute	Chronic	Total	Per Cent
Tricuspid.....	19	26	45	41.3
Pulmonic.....	3	1	4	3.3
Mitral.....	42	57	99	90.8
Aortic.....	20	43	63	57.7
Myocardium.....	46	28	74	67.8
Myocardium only.....	8	..	8	7.3
Pericardium.....	7	34	41	37.5

It will be noted that the myocardium alone was involved in eight cases. These have been included in the total of seventy-four instances of myocardial involvement. Wherever the lesion was in part acute and in part chronic, it has been listed only under the acute lesions. Included in this series are those cases of mitral stenosis without history of attacks of polyarthritis. Table 2 concerns the cases without a history of polyarthritis, with the distribution of the lesions found.

TABLE 2.—*Cases Without a History of Polyarthritis*

Rheumatic Disease of Heart			
Total number of cases.....			109
No history of joint involvement.....			41
Distribution of Lesions			
	Acute	Chronic	Total
Valves.....	19	14	33
Myocardium.....	19	5	24

Analysis of the series for the length of the interval between the last joint attack and the death of the patient shows some startling facts, especially with reference to the observation of acute lesions within the heart. The results of this analysis are given in table 3. Symbols used after the figures indicate cases in which acute lesions were found in more than one portion of the heart. If from this series of 109 cases, the total of forty-one cases without history of arthritis is deducted, it will be noted that of the sixty-eight patients with history of arthritis, thirty-five, or approximately 50 per cent, had intervals of from one to thirty-eight years of freedom from painful joints before death.

TABLE 3.—*Acute Rheumatic Lesions of the Heart*

Interval after Last Joint Involvement, Years	Endocardium		Myocardium			Pericardium	
			1	1"	3*	1"	2*
1.....		3*					
2.....	1	1*			1*		
3.....	2		2	1"		1"	
4.....		1*			1*		
5.....		1*			1*		
6.....	3	2*	1		2*	1	
8.....	1		1				
9.....						1	
10.....	1	2*	1		2*	1	
15.....	2		1				
20.....			1				
24.....			1				
34.....			1				
38.....			1				
Total, 35 cases							

* and " indicate cases in which acute lesions were found in more than one portion of the heart.

THE AORTA AND PERIPHERAL BLOOD VESSELS IN RHEUMATISM. ALWIN M. PAPPENHEIMER, New York.

It has been surmised for many years that the agent which causes rheumatic fever may affect the aorta or the peripheral blood vessels, but few careful studies of the subject have been made.

In a study of rheumatic aortitis seventy-seven cases were examined in which there was presumptive evidence of recent or old rheumatic infection, with an equal number of control cases in which there were neither clinical or pathologic indications of rheumatism. In addition to acute lesions, triangular or flame shaped scars have been found in about 40 per cent of the rheumatic cases and in less than 10 per cent of the control series, so that they are regarded as being diagnostically significant. The presence of Aschoff nodules in the adventitia or of the characteristic multinucleated cells is pathognomonic, but such lesions have been present in less than 15 per cent of the cases.

Lesions in the peripheral blood vessels have been found in ten of a series of forty-seven cases of rheumatic heart disease. These lesions are distinctive and do not fall within the rubric of hitherto described forms of arterial disease. It is a conviction, therefore, that the rheumatic agent may affect small peripheral blood vessels in many situations and may produce a distinctive form of arteriolitis or capillaritis.

Book Reviews

HISTOLOGICAL TECHNIQUE FOR NORMAL TISSUES, MORBID CHANGES AND THE IDENTIFICATION OF PARASITES. By H. M. CARLETON, M.A., B.Sc., PH.D., University Lecturer in Histology, Oxford. Chapters 7 and 8 in Collaboration with FREDERIC HAYNES, B.A., Demonstrator in Histology. Pp. 398, with 17 figures in the text. London: Humphrey Milford Oxford University Press, 1926 (Oxford Medical Publications).

This book succeeds in teaching things which generally cannot be taught but can be learned only by experience. It contains outlines of procedure for staining paraffin sections, for instance, which are useful to the beginner and to the experienced worker; the same is true of the "Table of Errors in Section Cutting, and Their Remedy" (page 81-82), of the chapter on dark-field examination and of the description of the way to obtain a good blood smear. The descriptions of the single steps in different procedures are clear, and the reader is told frequently that experience is necessary before good results can be expected regularly.

No one who works with tissues will ever be fully satisfied with the book of one of his colleagues; every one considers his own methods superior. For instance, the author recommends the rotary microtome and reserves the sliding microtome for special purposes; some, however, prefer the sliding microtome for routine work also because it gives better sections, and because the horizontal position of the block and knife affords a better view of the cutting surface. Besides, it is much more economical in using the edge of the knife, and with little experience it can be handled at least as fast as the rotary microtome. Furthermore, it enables one to handle different blocks individually by changing the speed of the cutting movement and the angle of the knife. Regaud's fluid is said (page 40) not to fix fat. This seems astonishing since Orth's mixture, which is practically identical, fixes fatty substances satisfactorily. Some of the methods described are complicated, while simpler ones give excellent results also, as shown in the part concerning serial sections on pages 78 and 83. On the other hand, the methods for the detection of eggs in fluids and in the feces are simple. Among the rapid methods for paraffin work, it would have been desirable to have the acetone methods mentioned because they give good staining results. Old yellow ammonium sulphide solution is recommended for the iron reaction; most workers use a solution which is only slightly yellow. No method is given for the staining of hemoglobin. On page 42, it is said that formalin inhibits carmine staining; but after carefully washing the material, satisfactory slides have been obtained with lithium carmine as well as with alum carmine. On page 321, formalin is recommended as fixative for bacterial stains; alcohol fixation is preferred by some, especially for staining tubercle bacilli. Among the methods for detecting fat embolism, the efficient, old, simple method of examining unstained sections which are cut by hand from the fresh organs deserves mention. The authors' critical standpoint on the subject of the staining of fat is pleasing. The chapter on pigments is probably so brief because of the chaotic condition of the present knowledge of pigments. A modification of the Gram method is mentioned (Claudius); it is said to

eliminate the possibility of over-differentiation. There is a large number of useful technical hints, and the book will prove a reliable aid in many situations.

The first twenty pages form a theoretical chapter on the cell and the protoplasm; this is rather instructive, but one does not see exactly its relation to the remainder of the book.

The use of the terms "eleidin" and "keratohyalin," on page 290, is questionable. Eleidin is said to occur in the stratum granulosum and to stain intensely with hematoxylin; keratohyalin is called the substance characteristic of the stratum lucidum. According to the opinion of others, eleidin belongs to the stratum lucidum and appears red in hematoxylin eosin slides while keratohyalin is characteristic of the stratum granulosum. The book states (page 307) that amyloid contains chondroitin sulphuric acid. This is not always the case. The origin of the hyaline casts in the urine, as given on page 312, is not certain. The substance found in the skin of myxedematous patients is probably not a true mucin.

The illustrations do not play an important rôle in such a book; the diagrammatic ones are good. A short bibliography is given, in which Spielmeier's manual might be included.

PRINCIPLES AND PRACTICE OF CHEMOTHERAPY WITH SPECIAL REFERENCE TO THE SPECIFIC AND GENERAL TREATMENT OF SYPHILIS. By JOHN A. KOLMER, M.D., PH.D., Professor of Pathology and Bacteriology in the Graduate School of Medicine, University of Pennsylvania. Pp. 1,106, with eighty-two illustrations. Cloth. Price, \$12, net. Philadelphia and London: W. B. Saunders, Company, 1926.

Kolmer's new book contains 1,100 closely written pages dealing with the subject of chemotherapy in its entirety, and as it is related to syphilis in particular.

The first 447 pages deal with practically every problem in chemotherapy so far investigated. These problems are discussed principally under the general heads of bacterial, trypanosomal, spirochetal and protozoan diseases. Under each heading the various diseases investigated are discussed in some detail and the various methods used in treating them experimentally are then fully described. The results obtained with various compounds follow, in well arranged order, and the practical application to clinical treatment is emphasized. A complete bibliography of the immediate subject discussed is given at the end of each chapter. The field of chemotherapy, embracing the work of investigators generally, describing methods, results and application, is treated far more completely in this section than in any other work which has yet appeared in this country.

The remainder of the volume deals particularly with syphilis, under the general headings of infection, immunity and pathology, pharmacology, toxicology and methods of administration of antisyphilitic compounds, and the prophylaxis and treatment, specific and nonspecific of syphilis.

The section on infection, immunity and pathology is comparatively brief, and in it the Wassermann reaction is discussed rather fully, particular emphasis being given to the author's new work in this field.

The section on pharmacology and toxicology deals with the antisyphilitic drugs far more extensively than any of the standard American works in this field, and deals with the toxicological aspect more fully than with the pharmacologic aspect. The whole subject of reactions, and their etiology, prevention and treatment is fully discussed.

The section on administration describes all acceptable methods for introducing the various antisyphilitic compounds into the host. The importance of proper technic in the preparation and administration of the powerful remedies used is emphasized, and the methods are set forth clearly both by illustration and by description. The greatest stress is laid on the correct administration of the "arsphenamines."

The last part of the book, 160 pages, deals with the practical treatment of syphilis. Prophylaxis in the usual sense, abortive treatment, nonspecific protein therapy and hygiene are discussed briefly but probably sufficiently. The advantages and disadvantages of the various organic arsenicals, mercurials, bismuth and iodine preparations are discussed. The specific treatment of syphilis in its various forms and stages is given in considerable detail, the author's methods being given prominence. The criteria given for prognosis and cure are somewhat exacting but are in keeping with the views of most authorities today.

This work of Kolmer's, while largely a digest of all work in the field of chemotherapy, particularly as relating to syphilis, also represents many contributions by the author. Indeed, it is astonishing to note how numerous are the problems which he and his associates have investigated. Consequently, while the work may appear to be unduly colored by the author's own observations and views, this can hardly be criticized, when his many years of assiduous and painstaking work in this field are considered. While the book is voluminous, the amount of material covered is enormous. The vast amount of detail on the experimental side, in comparison to the discussion on the practical management and treatment of syphilis, will preclude any popularization of the work so far as the general practitioner is concerned; it will, however, have a certain value in the hands of the syphilologist. It will be of particular value as a reference work to all interested or engaged in the field of chemotherapy and the study of antisyphilitic treatment. The references to the literature are extensive and complete, and the author appears to have expressed unusually well the essential observations and views of the various investigators.

Books Received

- LEAD POISONING. By JOSEPH C. AUB, LAWRENCE T. FAIRHALL, A. S. MINOT and PAUL REZNIKOFF. With a chapter on the Prevalence of Industrial Lead Poisoning in the United States by ALICE HAMILTON. Pp. 265. Price, \$4. Baltimore: Williams & Wilkins Company, 1926.
- PNEUMOCONIOSIS (SILICOSIS). A ROENTGENOLOGICAL STUDY WITH NOTES ON PATHOLOGY. By HENRY K. PANCOAST and EUGENE P. PENDERGRASS, Philadelphia. Pp. 186. Price, \$4. New York: Paul B. Hoeber, 1926.
- PHYSIOLOGY AND BIOCHEMISTRY IN MODERN MEDICINE. By J. J. R. MACLEOD, Professor of Physiology in the University of Toronto, Toronto, Canada, assisted by ROY G. PEARCE, A. C. REDFIELD, N. B. TAYLOR, J. M. D. OLMSTED and others. Fifth edition, with 291 illustrations, including 9 plates in color. Price, \$11. St. Louis: C. V. Mosby Company, 1926.
- HUMAN PATHOLOGY: A Textbook. By HOWARD T. KARSNER, Professor of Pathology, School of Medicine, Western Reserve University, Cleveland, with an introduction by SIMON FLEXNER. Pp. 980, with 20 illustrations in color, and 443 in black and white. Price, \$10. Philadelphia & London: J. B. Lippincott Company, 1926.
- PROTOZOOLOGY: A Manual for Medical Men, Veterinarians and Zoologists. By C. M. WENYON (LONDON), Director-in-Chief of the Wellcome Bureau of Scientific Research, formerly protozoologist to the London School of Tropical Medicine. In two volumes, with 565 illustrations and 20 colored plates. Pp. 1,563. Price, \$25. New York: William Wood & Co., 1926.
- LA ROUGEOLE, ÉPIDÉMIOLOGIE, IMMUNOLOGIE, PROPHYLAXIE. Par ROBERT DEBRÉ and PIERRE JOANNON. Préface Du LEON BERNARD. Pp. 288. Paris: Masson et Cie, 1926.
- LOCAL IMMUNIZATION. By PROF. A. BESREDKA, Pasteur Institute, Paris, edited and translated by DR. HARRY PLOTZ, Pasteur Institute, Paris. Pp. 181. Price, \$2.50. Baltimore: Williams & Wilkins Company, 1927.
- THE SIGNIFICANCE OF THE PHYSICAL CONSTITUTION IN MENTAL DISEASE. By F. I. WERTHEIMER and FLORENCE E. HESKETH, with a preface by LEWELLYS F. BARKER. Pp. 76. Price, \$2.50. Baltimore: Williams & Wilkins Company, 1927.
- TUBERCULOSIS BACTERIOLOGY, PATHOLOGY AND LABORATORY DIAGNOSIS WITH SECTIONS ON IMMUNOLOGY, EPIDEMIOLOGY, PROPHYLAXIS AND EXPERIMENTAL THERAPY. By EDWARD R. BALDWIN, S. A. PETROFF and LEROY S. GARDNER. Pp. 342. Price, \$4.50. Philadelphia: Lea & Febiger, 1927.
- GRUNDRISSE DER PATHOLOGISCHEN ANATOMIE. VON PROF. DR. GOTTHOLD HERXHEIMER, Prosektor am Städt. Krankenhaus zu Wiesbaden. Allgemeiner Teil, mit 466 zum grossen Teil farbigen Abbildungen. Neunzehnte Auflage des Schmaus'schen Grundrisses der path. Anat. Pp. 312. Price, 28.80 marks. Munich: J. F. Bergman, 1927.

THE AMERICAN PATHOLOGICAL AND LABORATORY MEDICAL ASSOCIATION, as organized in the United States and Canada, observes the following:

Manuscripts for publication should be sent to Dr. Ludwig Chicago, or to other members of the Association, regarding the following: *Pathology and Laboratory Medicine*, American Medical Association, Dearborn, Ill., Chicago.

Articles are accepted for publication on a sole basis to the *AMERICAN PATHOLOGICAL AND LABORATORY MEDICAL ASSOCIATION*. Manuscripts must be typewritten, preferably on one space, submitted in triplicate, and the name of the publisher, who is the original proprietor, must be stated.

Footnotes and bibliographies should be Cumulative and published by the American Association in order to give the author credit of article, page, number, month, year—and year for standard of article, together with a list of A. M. A. publications. The Art of comprehensive and the publication of American Association, Chicago, Ill., \$1.50.

Matter appearing in the *AMERICAN PATHOLOGICAL AND LABORATORY MEDICAL ASSOCIATION* is covered by copyright, but, as a rule, no objection is raised to medical journals if printed reproduction is for commercial purposes of *PATHOLOGY AND LABORATORY MEDICINE*, or in the *AMERICAN PATHOLOGICAL AND LABORATORY MEDICAL ASSOCIATION* will not be granted.

Authors who give one hundred reprints obtained in the *AMERICAN PATHOLOGICAL AND LABORATORY MEDICAL ASSOCIATION*.

The *AMERICAN PATHOLOGICAL AND LABORATORY MEDICAL ASSOCIATION* price (two volumes): design, postage, single copy. Check should be made payable to the *AMERICAN PATHOLOGICAL AND LABORATORY MEDICAL ASSOCIATION*.

is published by the *AMERICAN PATHOLOGICAL AND LABORATORY MEDICAL ASSOCIATION* for the advance the *AMERICAN PATHOLOGICAL AND LABORATORY MEDICAL ASSOCIATION* of the *AMERICAN PATHOLOGICAL AND LABORATORY MEDICAL ASSOCIATION*.

Manuscripts for publication should be sent to Dr. Ludwig Chicago, or to other members of the Association, regarding the following: *Pathology and Laboratory Medicine*, American Medical Association, Dearborn, Ill., Chicago.

Articles are accepted for publication on a sole basis to the *AMERICAN PATHOLOGICAL AND LABORATORY MEDICAL ASSOCIATION*. Manuscripts must be typewritten, preferably on one space, submitted in triplicate, and the name of the publisher, who is the original proprietor, must be stated.

Footnotes and bibliographies should be Cumulative and published by the American Association in order to give the author credit of article, page, number, month, year—and year for standard of article, together with a list of A. M. A. publications. The Art of comprehensive and the publication of American Association, Chicago, Ill., \$1.50.

Matter appearing in the *AMERICAN PATHOLOGICAL AND LABORATORY MEDICAL ASSOCIATION* is covered by copyright, but, as a rule, no objection is raised to medical journals if printed reproduction is for commercial purposes of *PATHOLOGY AND LABORATORY MEDICINE*, or in the *AMERICAN PATHOLOGICAL AND LABORATORY MEDICAL ASSOCIATION* will not be granted.

Authors who give one hundred reprints obtained in the *AMERICAN PATHOLOGICAL AND LABORATORY MEDICAL ASSOCIATION*.

The *AMERICAN PATHOLOGICAL AND LABORATORY MEDICAL ASSOCIATION* price (two volumes): design, postage, single copy. Check should be made payable to the *AMERICAN PATHOLOGICAL AND LABORATORY MEDICAL ASSOCIATION*.

OTHER PERIODICAL PUBLICATIONS of the American Medical Association

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION—Weekly. Published by the American Medical Association, 535 North Dearborn, Chicago, Ill. Single copy, 10¢; foreign, 15¢.

ARCHIVES OF INTERNAL MEDICINE—Monthly. Published by the American Medical Association, 535 North Dearborn, Chicago, Ill. Single copy, 10¢; foreign, 15¢.

AMERICAN JOURNAL OF DISEASES OF CHILDREN—Monthly. Published by the American Medical Association, 535 North Dearborn, Chicago, Ill. Single copy, 10¢; foreign, 15¢.

ARCHIVES OF PEDIATRICS AND PEDIATRIC SURGERY—Monthly. Published by the American Medical Association, 535 North Dearborn, Chicago, Ill. Single copy, 10¢; foreign, 15¢.

ARCHIVES OF DERMATOLOGY AND SYPHILIS—Monthly. Published by the American Medical Association, 535 North Dearborn, Chicago, Ill. Single copy, 10¢; foreign, 15¢.

AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY—Monthly. Published by the American Medical Association, 535 North Dearborn, Chicago, Ill. Single copy, 10¢; foreign, 15¢.

ARCHIVES OF LARYNGOLOGY—Monthly. Published by the American Medical Association, 535 North Dearborn, Chicago, Ill. Single copy, 10¢; foreign, 15¢.

ARCHIVES OF RELATIVE SURGERY—Monthly. Published by the American Medical Association, 535 North Dearborn, Chicago, Ill. Single copy, 10¢; foreign, 15¢.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION—Weekly. Published by the American Medical Association, 535 North Dearborn, Chicago, Ill. Single copy, 10¢; foreign, 15¢.

ARCHIVES OF INTERNAL MEDICINE—Monthly. Published by the American Medical Association, 535 North Dearborn, Chicago, Ill. Single copy, 10¢; foreign, 15¢.

AMERICAN JOURNAL OF DISEASES OF CHILDREN—Monthly. Published by the American Medical Association, 535 North Dearborn, Chicago, Ill. Single copy, 10¢; foreign, 15¢.

ARCHIVES OF PEDIATRICS AND PEDIATRIC SURGERY—Monthly. Published by the American Medical Association, 535 North Dearborn, Chicago, Ill. Single copy, 10¢; foreign, 15¢.

ARCHIVES OF DERMATOLOGY AND SYPHILIS—Monthly. Published by the American Medical Association, 535 North Dearborn, Chicago, Ill. Single copy, 10¢; foreign, 15¢.

AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY—Monthly. Published by the American Medical Association, 535 North Dearborn, Chicago, Ill. Single copy, 10¢; foreign, 15¢.

ARCHIVES OF LARYNGOLOGY—Monthly. Published by the American Medical Association, 535 North Dearborn, Chicago, Ill. Single copy, 10¢; foreign, 15¢.

ARCHIVES OF RELATIVE SURGERY—Monthly. Published by the American Medical Association, 535 North Dearborn, Chicago, Ill. Single copy, 10¢; foreign, 15¢.

